A STUDY OF THE EPOXIDE LINKAGE AS A TYPE OF NEIGHBORING GROUP IN NUCLEOPHILIC DISPLACEMENT REACTIONS

by

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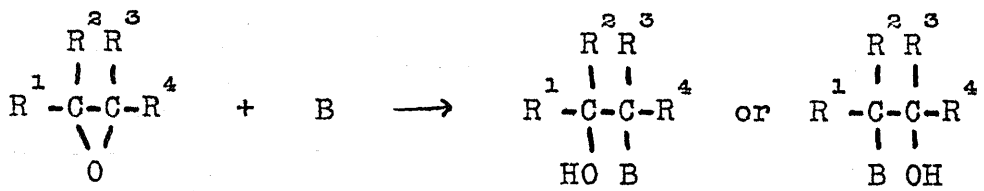
INTRODUCTION AND STATEMENT OF PROBLEM

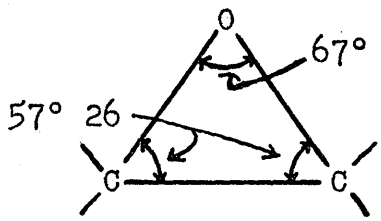
Widespread heightened interest in the chemistry of the epoxides is indicated by the ever-increasing number of publications in this field during the last twenty years. The epoxides are of intense interest because they can be made to react with a great variety of compounds, giving many products of value as intermediates in synthetic and industrial chemistry.

From a theoretical standpoint, epoxides are very interesting compounds since they lend themselves to kinetic studies without the necessity of kinetic measurements. The reactions of unsymetrical epoxides can result in either of two products depending on which end of the epoxide function is attacked, and since the reaction is irreversible, the



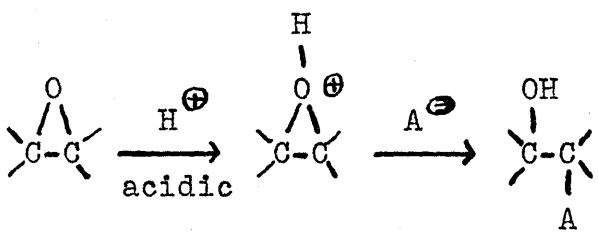
relative rates of attack at these two points is directly proportional to the relative amounts of the two products formed. The experimental conditions are identical for attack at either position. Thus, the relative electronic or steric effects of different groups can be studied by attaching these groups to the epoxide ring and studying their influence on the direction of ring opening. Several such studies have been conducted.[1,2,3,4]

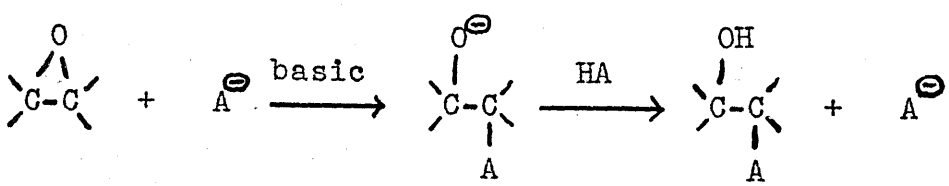
Ethylene oxides, or more commonly known simply as epoxides, make up one of the most simple classes of heterocyclic compounds. They owe their reactivity to a strained ring of two carbon atoms and one oxygen atom. Electron diffraction studies[5,6] on ethylene oxide and the cis and trans 2,3-epoxybutanes show that the interatomic distances are normal. It was also shown that the bond angle of the oxygen atom is reduced to 67° and the bond angles at the carbon atoms are 57° 26' as compared to the normal 109° 28'. Bonds under



such a strain are easily broken. Epoxides have only very small dipole moments. Ethylene oxide and propylene oxide give values of 1.88×10^{-18} e.s.u.[7,8]

All of the reactions of epoxides involve a breaking of one of the carbon-oxygen bonds. This can be done under either acidic or basic conditions.





The type of reaction which was studied in this work is the reaction of alphabromoepoxides, R-CH-CH-CHBr-R, with
O
relatively strong bases under S_N2 conditions. In the S_N2 mechanism,[9] the driving force is a "push" or nucleophilic attack by the entering atom or group, which has an unshared pair of electrons that it is eager to donate in bond formation. The attack is entirely from the back side and causes inversion at the carbon atom involved. It appears to be second order kinetically. Generally, "S_N2 conditions" infers the use of a nonsolvating solvent; that is, a solvent which is not strongly enough electrophilic to cause a preliminary ionization of the group to be displaced. When such ionization is the first step of the reaction, the mechanism is called S_N1 and the reaction appears to be first order, the rate determining step being the ionization.

In some recent articles, Swain[10] has advanced the theory that all nucleophilic displacement reactions are actually termolecular, involving both the "push" attributed to the S_N2 mechanism and the "pull" of the S_N1 mechanism. According to this theory, the order of the reaction depends on whether or not the concentration of the reactants changes appreciably during the reaction. The solvent is usually present in large excess and has no apparent effect on the rate. The S_N1 mechanism seems to be an extreme case that is apparent when the "pull" exerted by the solvent is very much more effective than the "push" exerted by the entering base. Likewise, the

S_N2 mechanism is apparent in cases where the solvating effect is much weaker than the "push" of the basic attacking group. These conditions were used instead of S_N1 conditions because under S_N1 conditions the epoxide ion formed in the first step would be neutralized before it had a chance to displace the bromide ion.

The purpose of this work was to study the effect of the epoxide linkage as a neighboring group[a] in nucleophilic displacement reactions. Considerable work has been done in recent years on the neighboring group effect and many different groups have been shown to exert an effect on this type of reaction. In many reactions, the rates and steric results cannot be explained without considering the effects of neighboring groups other than their effects as suppliers or withdrawers of electrons to or from the point of attack. One effect is that of actual participation of a group on a carbon atom in a displacement process at that carbon atom. Thus, a displacement reaction might consist of two steps, the first an intramolecular S_N2 reaction, and the second the opening of the ring.[11] Two inversions and apparent retention will be the steric result.

The following mechanism, which has been proposed by Winstein and Lucas[12] for the reaction of hydrogen bromide with a bromohydrin, demonstrates this effect.

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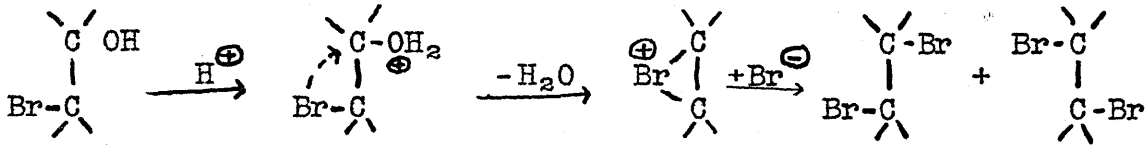
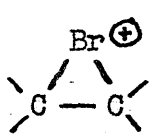
a. The epoxide linkage is not a typical neighboring group since it cannot function in this manner until a basic attack has broken one of the carbon-oxygen bonds. The term is used here because it best describes the second step of these reactions.



Evidence cited for this mechanism is the fact that complete retention of configuration is observed.

The fact that bromine addition to olefins results in predominantly the trans product is attributed to the formation of a three membered ring of two carbon atoms and the bromonium ion, which is then opened by an attack of the bromide ion.[13,14] Lucas and Gould have presented evidence for an analagous chloronium ion.[15]

According to Winstein and Buckles,[11] the reactions of silver acetate in dry acetic acid with the erythro- and threo-2-acetoxy-3-bromobutanes, trans-1-acetoxy-2-bromo-cyclohexane, the meso- and dl-2,3-dibromobutanes, and trans-1,2-dibromo-cyclohexane proceed with predominant retention of configuration. Also, optically active 2,3-dibromobutane and trans-1-acetoxy-2-bromocyclohexane give rise to completely inactive diacetates. The steric results are believed to be due to participation of a neighboring bromine or acetoxy group in the displacement processes, with production of the intermediates,



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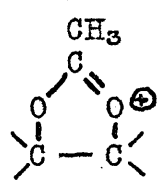
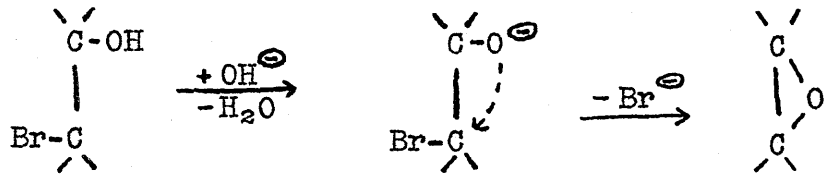


This neighboring group effect has been reported to take place in both S_N1 and S_N2 reactions.[16] Some recent kinetic studies give further evidence in favor of these mechanisms.[17,18,19]

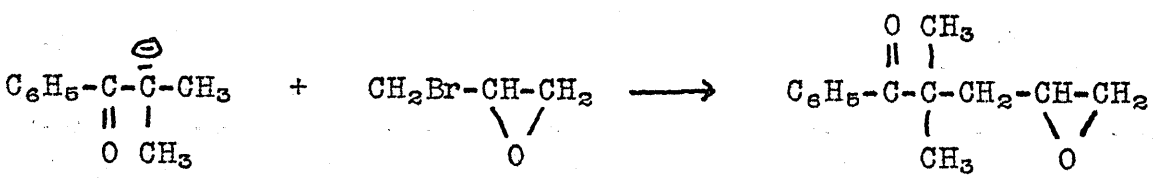
The formation of epoxides from halohydrins is also believed to proceed by this mechanism.[13] The oxide formed by



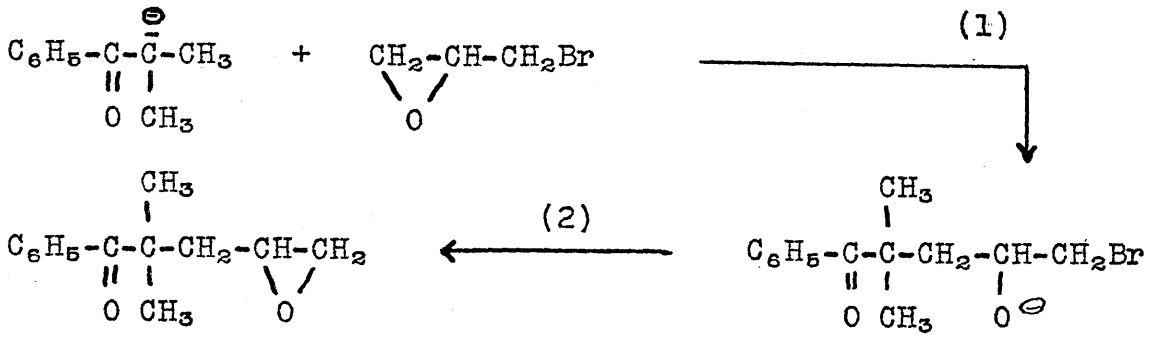
removal of a proton by the hydroxyl ion, acts as a neighboring group and displaces the bromide ion from the adjacent carbon atom. This causes an inversion of configuration at the carbon atom from which the bromine atom is removed.

The present plan was to open an epoxide ring by an attack with a basic anion and see if the epoxide ion formed would in turn displace the alpha-bromine atom by this so-called neighboring group effect.

Up to the present time, very little work has been done on this type of reaction. In 1914, Haller and Ramart-Lucas[20] reported the reaction of isobutyrophenone anion with epibromohydrin and isolated as the product of the reaction, the epoxide shown.

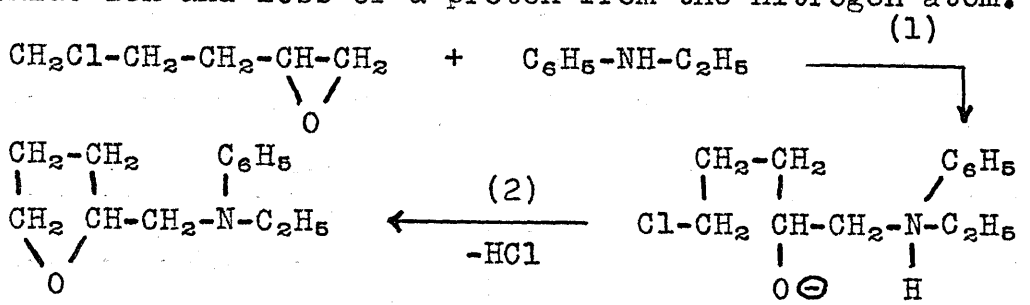


This reaction was interpreted as proceeding by a simple nucleophilic displacement of the bromide ion by the isobutyrophenone carbanion. However, it should be noted that exactly the same product would result from a two-step reaction involving (1) the attack of the carbanion at the terminal carbon of the epoxide followed by (2) a neighboring group displacement of the bromide ion by the oxide ion.



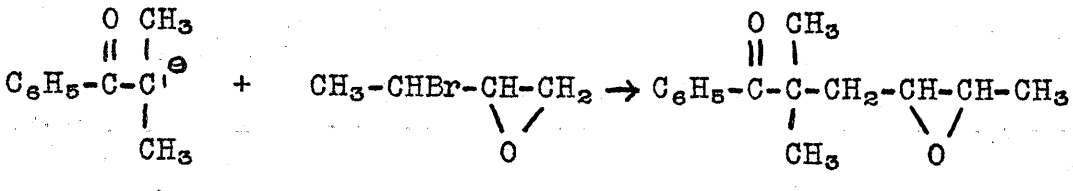
Step (2) is identical with the postulated mechanism for the synthesis of epoxides by the dehydrohalogenation of halohydrins, as shown above. Since epoxides are so very highly reactive because of the strained ring, this neighboring group mechanism seems preferable to the simple bromide ion displacement postulated by Haller and Ramart-Lucas. Unfortunately, this assumption cannot be proved in the case of epibromohydrin which would give the same product by either mechanism.

In 1947, Paul and Tchelitcheff[21] reacted 5-chloro-1,2-epoxypentane with phenylethylamine and obtained as a product, phenylethyltetrahydrofurfurylamine. This reaction can be interpreted as proceeding by a neighboring group mechanism similar to that explained above, involving (1) an attack of the basic amine on the terminal carbon of the epoxide group followed by (2) a displacement of the chloride ion by the alkoxide ion and loss of a proton from the nitrogen atom.



This work of Paul and Tchelitcheff shows the formation of a five-membered ring, which is notably very stable. The formation of a three-membered ring, which is under considerable strain, might seem, at first glance, to be more difficult. However, in forming the three-membered ring, the close proximity of the alkoxide ion to the carbon atom holding the halogen causes the probability of collision to be much greater and hence the three-membered ring may be just as easy to form.

Russell and Vander Werf[22] studied the reaction of isobutyrophenone carbanion with two alphabromoepoxides, 1-bromo-2,3-epoxybutane and 3-bromo-1,2-epoxybutane. From their results, they were led to believe that with the terminal epoxide a neighboring group effect did take place as shown below. However, with the other bromoepoxide, a simple bromide ion displacement is believed to have occured.



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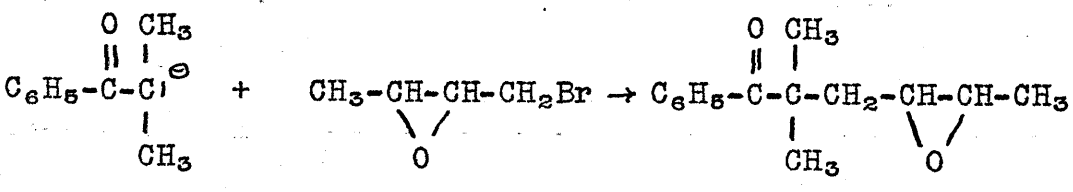


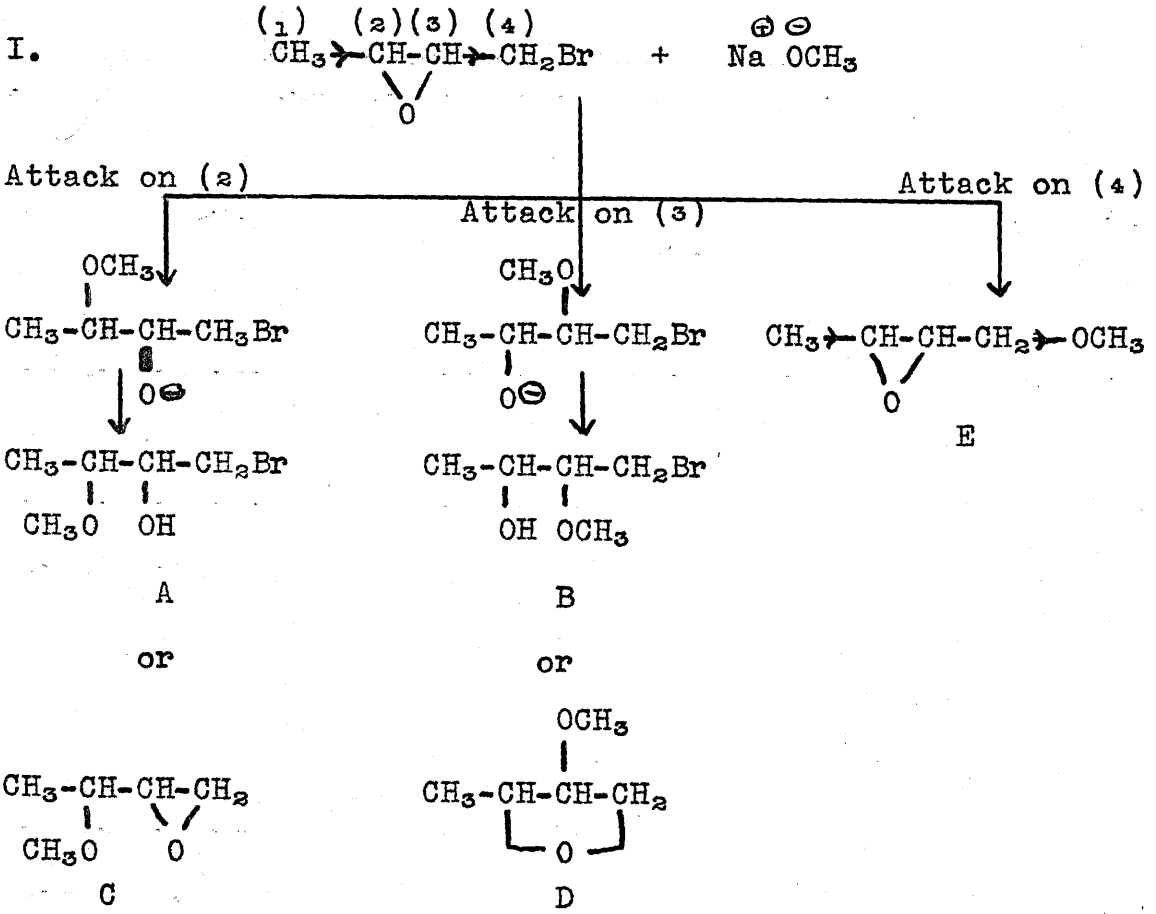
III IV

Products II and IV were proved to be isomers by analysis and both gave the same carboxylic acid when oxidized. The two compounds were not identical since they had different boiling points but they were believed to be geometrical isomers.

Russell and Vander Werf believed that the reason a neighboring group effect was not observed in the second reaction was that the isobutyrophenone carbanion was too large and its steric requirements would not allow it to attack the epoxide linkage. Hence, it attacked the less hindered carbon atom bearing the bromine atom.

In the present study the smaller bases, methoxide and ethoxide ions, were treated with the same two alphabromoepoxides. These bases are much smaller and would have a much better chance to attack the epoxide linkage and cause a neighboring group effect with both alphabromoepoxides.

The possible products of the reactions of these epoxides with sodium methoxide are listed below. Those from the ethoxide reactions would be analogous.



Products C, D and E are capable of reacting further with methoxide ion.

C + $CH_3O^{\ominus}$ ⟶ $CH_3-\underset{\underset{CH_3O}{|}}{CH}-\underset{\underset{OCH_3}{|}}{CH}-CH_2-OH$ (F) or $CH_3-\underset{\underset{CH_3O}{|}}{CH}-\underset{\underset{OH}{|}}{CH}-\underset{\underset{OCH_3}{|}}{CH_2}$ (G)

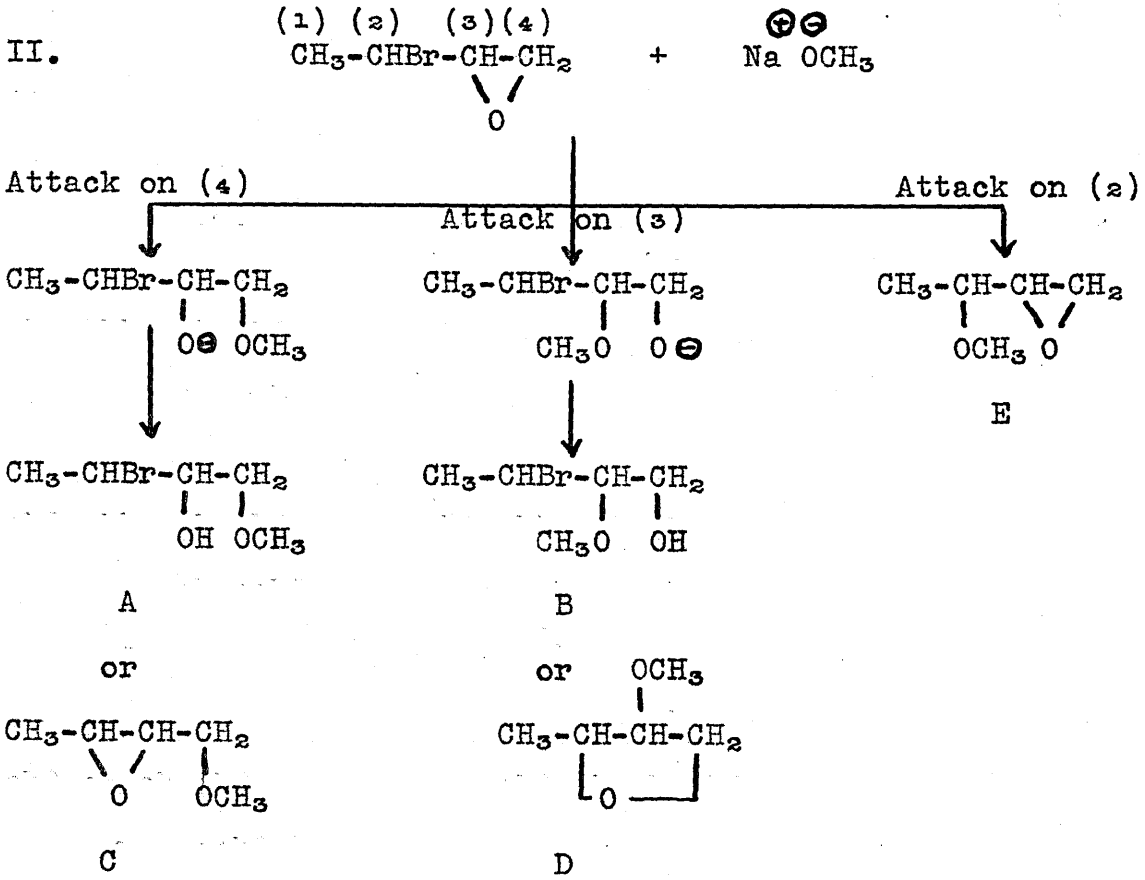
D + $CH_3O^{\ominus}$ ⟶ $CH_3-\underset{\underset{CH_3O}{|}}{CH}-\underset{\underset{OCH_3}{|}}{CH}-CH_2-OH$ (H) or $CH_3-\underset{\underset{OH}{|}}{CH}-\underset{\underset{OCH_3}{|}}{CH}-CH_2-OCH_3$ (J)

E + $CH_3O^{\ominus}$ ⟶ $CH_3-\underset{\underset{OH}{|}}{CH}-\underset{\underset{OCH_3}{|}}{CH}-CH_2-OCH_3$ (K) or $CH_3-\underset{\underset{CH_3O}{|}}{CH}-\underset{\underset{OH}{|}}{CH}-\underset{\underset{OCH_3}{|}}{CH_2}$ (L)

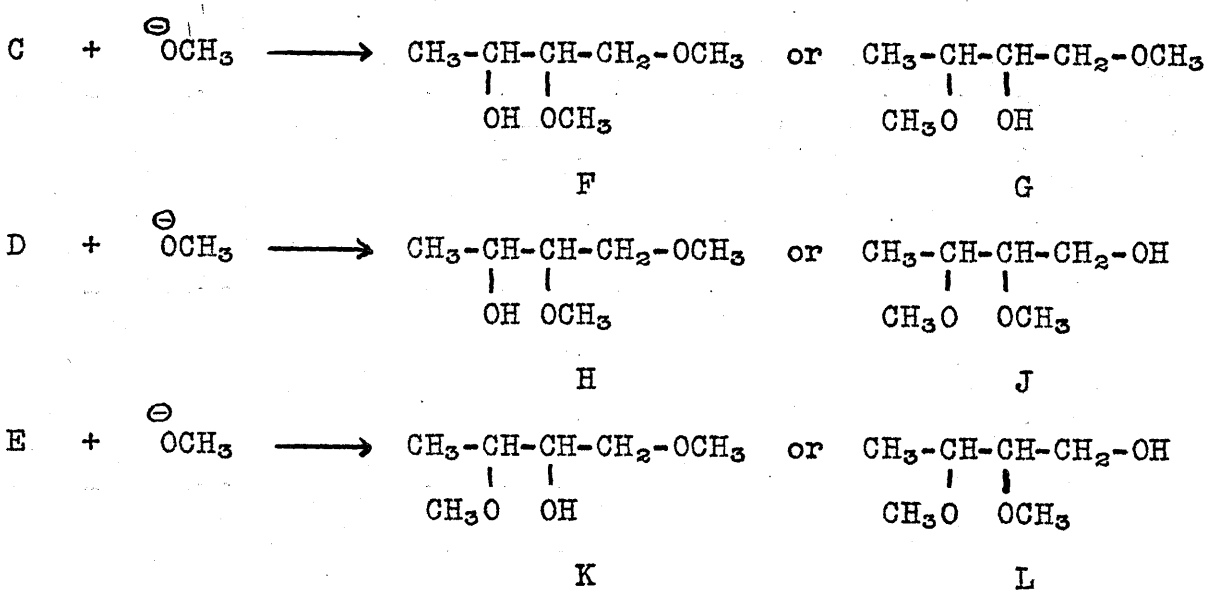
If the epoxide linkage were attacked first, it would be very probable that the epoxide ion intermediate would replace the bromine atom rather than becoming neutralized by picking up a proton from the solvent. Thus, products A and B are ruled as improbable. From an electronic standpoint, carbon atom (3) would be more positive than (2) and thus more vulnerable to basic attack. Thus, if the epoxide ring were attacked in preference to the halogenbearing carbon, product D would be the preferred product. However, trimethylene oxide rings are noteably hard to form. If the bromine were displaced first, product E would result.

Of the two secondary products from D, J would be the expected product, both electronically and sterically. From E, the product favored electronically would be K (identical to J) because carbon (3) is more positive and more vulnerable to basic attack than carbon (2) due to the inductive effects of the methyl and methoxymethyl groups.

The possible products from the other epoxide are as follows:

II. 

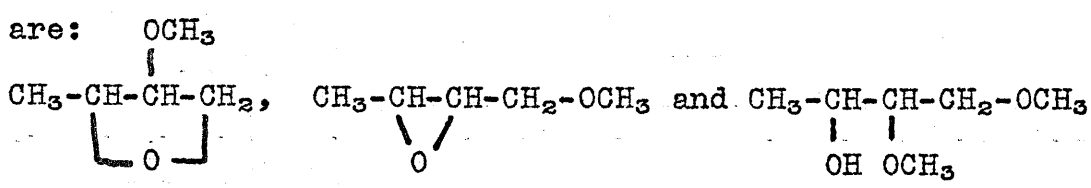
Again, products C, D and E are capable of reacting further with methoxide.



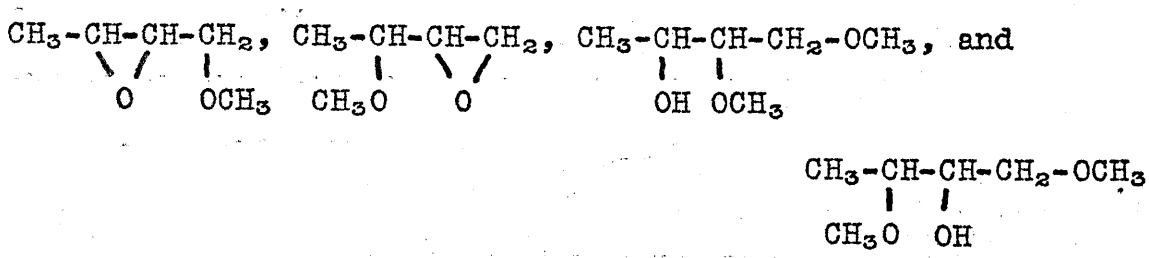
Products A and B are ruled improbable on the same

grounds as they were in reaction I. If the epoxide linkage were attacked first, carbon (4) would be the preferred point of attack since in reactions of terminal epoxides with bases, almost invariably the terminal carbon atom is attacked.[23] Thus, product C would be expected. If the bromine were displaced directly product E would result. Of the secondary products from C, product F would be expected, for the same reasons given for expecting K from E in reaction I. From E, the expected secondary product would be K, since E is a terminal epoxide.

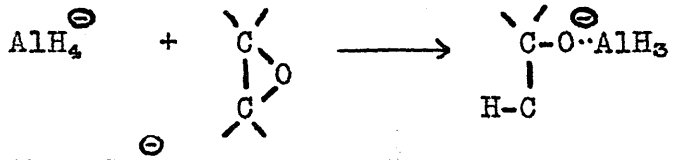
Summarizing, the most probable products from reaction I are:



From reaction II they are:

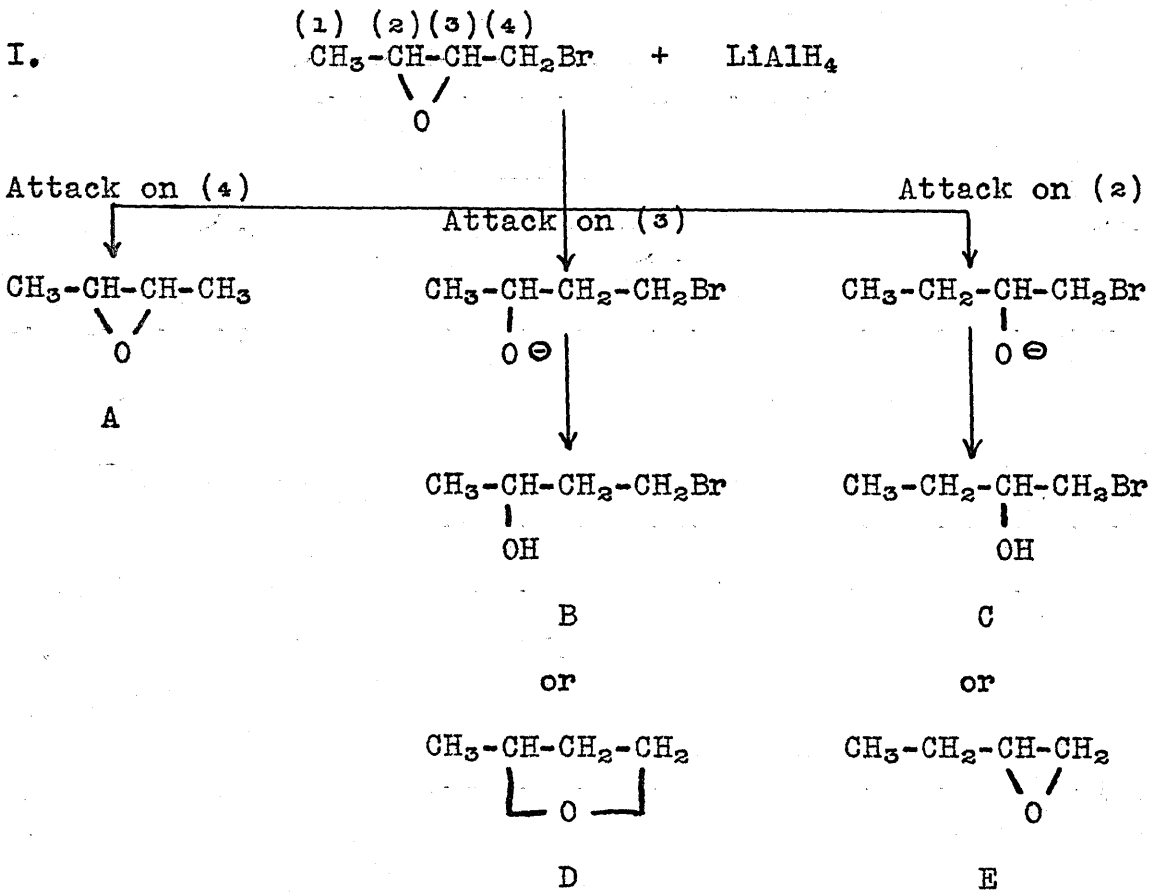


The two bromoepoxides were also reacted with lithium aluminum hydride, whose reactions have many features in common with the familiar nucleophilic displacement mechanism. The exact nature of the attacking group is not known definitely but is believed by some to be a series of complex aluminohydride ions,[24] $AlH_4^{\ominus}$, $AlXH_3^{\ominus}$, $AlX_2H_2^{\ominus}$ and $AlX_3H^{\ominus}$ where X denotes an alkoxide ion with which the aluminum atom coordinates. The first step of the reaction with epoxides can be pictured as proceeding thus:

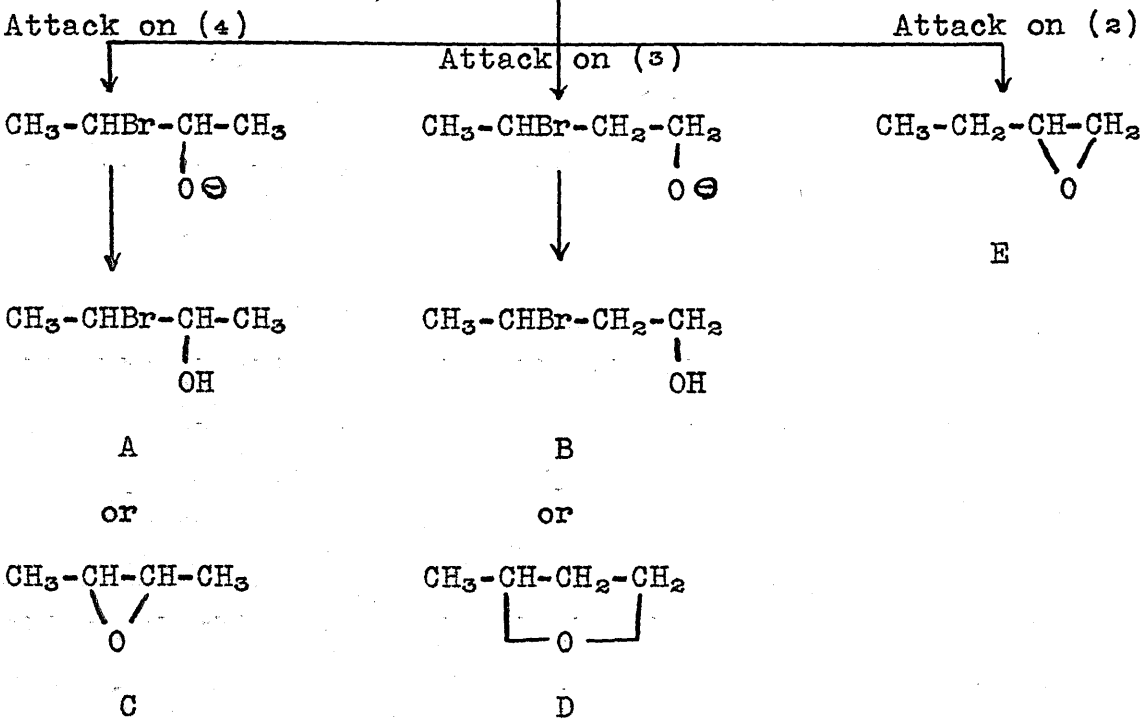


After all of the $AlH_4^{\ominus}$ is used up, the attacking group is thought to be $AlH_3X^{\ominus}$, which is a rather large group. This reagent also reduces organic halides, replaceing the halogen atom in the organic molecule with a hydrogen atom. Thus, the reaction is again a competition of bromide and epoxide.

A series of possible products can be formulated analogous to those proposed for the reactions of sodium methoxide, differing only in that these would have hydrogen atoms in place of the methoxy groups.



II. $CH_3-CHBr-CH-CH_2$ (1) (2) (3)(4) + $LiAlH_4$



All five possible products from both reactions should give 2-butanol upon reaction with a second mole of lithium aluminum hydride.

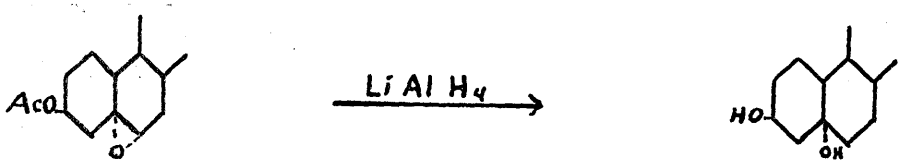
$$\text{I(A,B,C,D,E) and II(A,B,C,D,E)} \xrightarrow{LiAlH_4} CH_3-CH_2-CH(OH)-CH_3$$

In reaction I, just as in the methoxide and ethoxide reactions, if the epoxide were attacked first, carbon atom (3) is more vulnerable from an electronic point of view than carbon (2). This would make B and D more probable than A. Of these two, D would be preferred over B. If the halogen bearing carbon is attacked first, the expected product would be E.

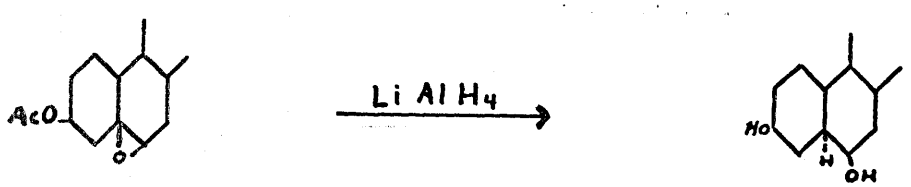
In reaction II, if the epoxide is attacked first the terminal carbon is most vulnerable[25] and the expected product

is C. Thus C and E are the most probable products.

The interpretation above is based entirely on electronic aspects. However, in view of the large size of the nucleophilic group, steric aspects may be quite important. Several terminal epoxides have been reduced with lithium aluminum hydride[25] and in all cases, a terminal attack is predominant. There are only a few instances reported in the literature of the reduction of other than terminal epoxides.[26,27,28] Among these, there are two cases which show quite definitely that steric hindrance is important. Plattner, Heusser and Feurer[23] reported the reduction of alpha- and beta-cholesterol acetates from which they obtained 3(β)-5(α)-dihydroxycholestane and 3(β)-6(β)-dihydroxycholestane respectively.



Alpha-Cholesterol Acetate 3(β)-5(α)-Dihydroxycholestane

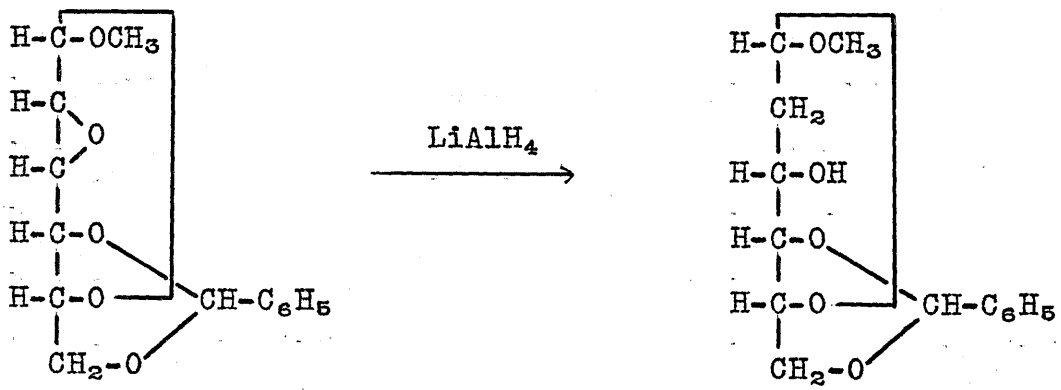


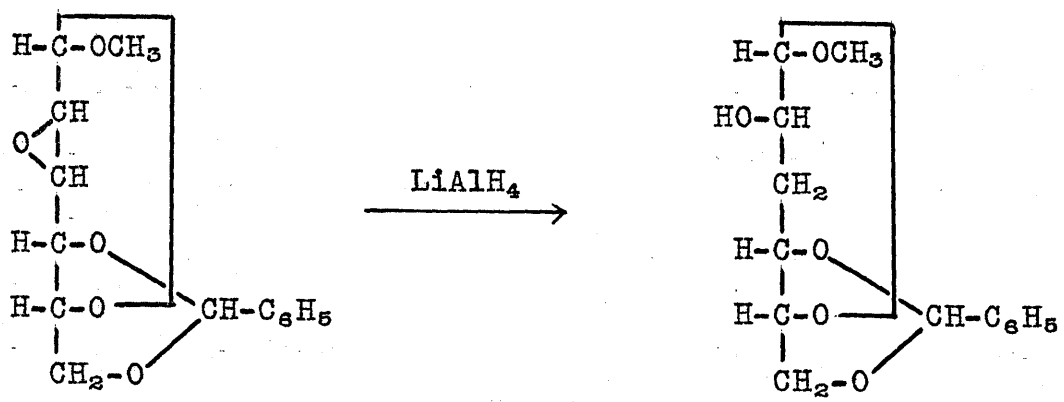
Beta-Cholesterol Acetate 3(β)-6(β)-Dihydroxycholestane

It is interesting that in the reduction of beta cholesterol acetate, in which the 3-acetoxy and the 5,6-epoxy groups are on the same side of the molecule, the product is 3(β)-6(β)-dihydroxycholestane, which would be obtained by attack on carbon atom 5. However, when the 3-acetoxy and 5,6-epoxy groups are on opposite sides of the molecule as in alpha-

cholesterol acetate, the product is 3(β)-5(α)-dihydroxy-cholestane which would be obtained by an initial attack on carbon 6. This might be interpreted as being caused by the steric effect of the acetoxy group. When it is on the opposite side of the molecule from the epoxide, it is in position to block an attack on that side of carbon 5, and thus the attack is on carbon 6. However, when it is on the same side of the molecule as the epoxide group, it cannot get into position to block the attack.

Prins[26] reported the reduction of the following two isomeric epoxides with lithium aluminum hydride. When the





methoxy group is on the same side of the ring as the epoxide group, the attack is on carbon atom 2, adjacent to the methoxy group, giving the 3-carbinol. However, when the

methoxy group is on the opposite side of the ring from the epoxide, the attack comes on carbon atom 3, giving the 2-carbinol. Since the only difference in the two molecules is the relative positions of the methoxy and epoxy groups, the only plausible explanation for these results is that the methoxy group, when on the opposite side of the ring blocks the back-side attack on the nearest end of the epoxide linkage. However, when on the same side, it cannot block the attack and the normal attack occurs.

Studies with molecular models show that a methoxy group, attached to a carbon atom adjacent to an epoxide group, is large enough to block an attack on the near end of the epoxide.

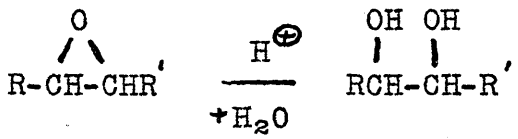
Another part of the problem consisted of working up a method for the quantitative determination of epoxides. There are several such determinations reported in the literature [29,30,31,32,33] but all of them are either inconvenient to use or are adaptable only to specific epoxides. A method which is easy to use and generally adaptable to most epoxides is highly desirable.

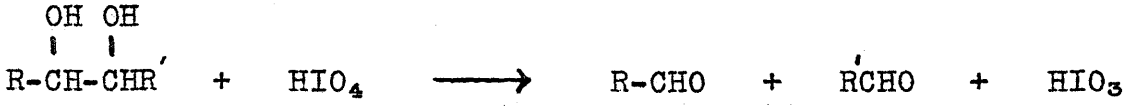
Eastham and Latremouille[28] had reported the use of periodic acid in the determination of ethylene oxide but they made no attempt to extend this to other epoxides. This method was tried on several other epoxides.

The determination is based on two well known reactions. The first is the acid catalyzed opening of an epoxide ring by water to give a glycol.[34] The second is the cleavage of

the glycol with periodic acid to give two aldehydes.[35]

A known quantity of periodic acid is used and the excess is

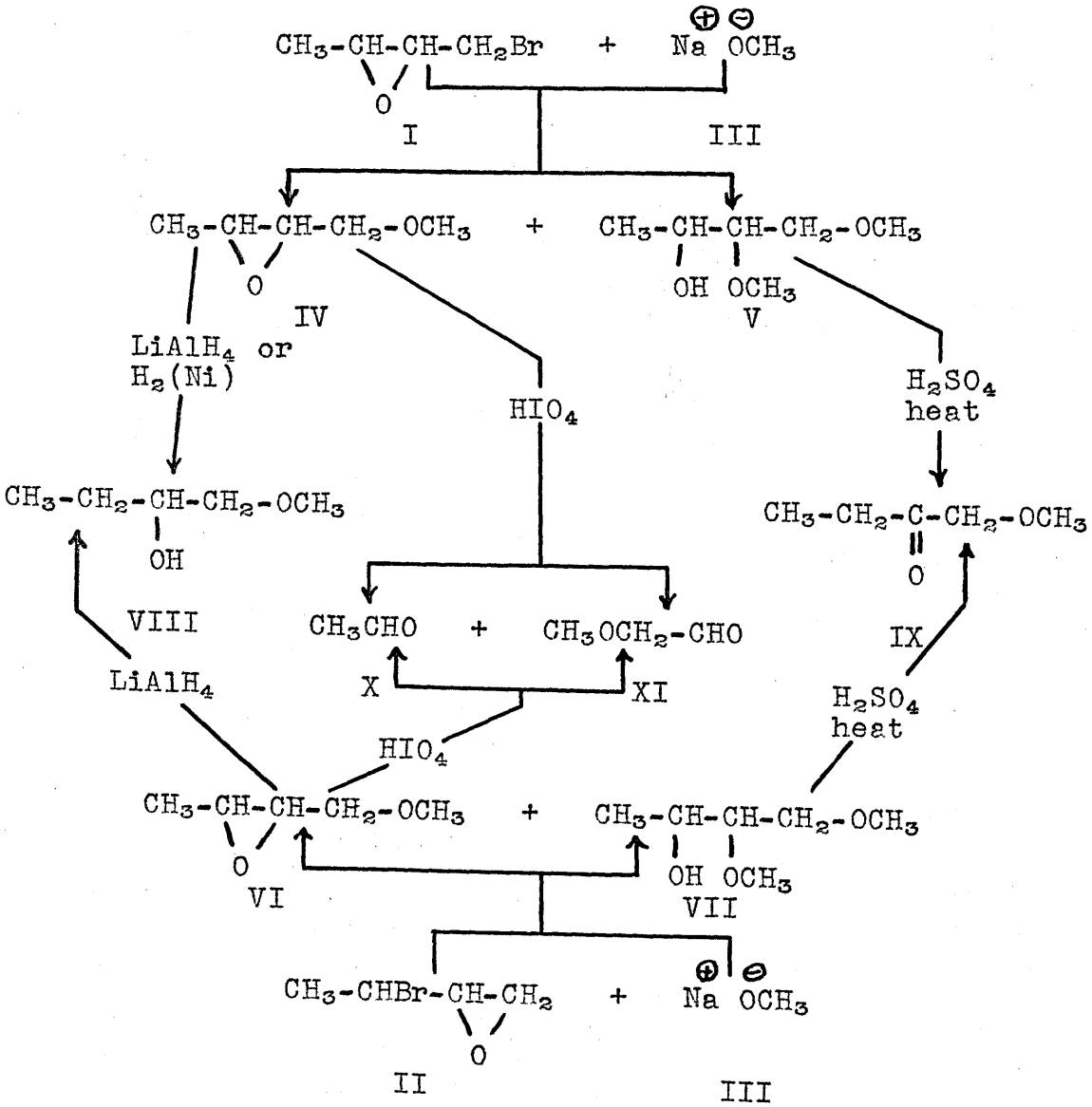




determined by an iodimetric procedure outlined by Fleury.[36]

RESULTS

The compounds, 1-bromo-2,3-epoxybutane, I, and 3-bromo-1,2-epoxybutane, II, prepared by the method described by Petrov,[37] were treated with sodium methoxide in absolute methanol. These primary reactions and the main reactions used in the proof of structure of the products are depicted graphically below.



$$CH_3\text{-}CH{=}CH\text{-}CH_2\text{-}OCH_3 \xrightarrow[2.\ KOH]{1.\ HOCl} CH_3\text{-}CH\text{-}CH\text{-}CH_2OCH_3 \quad (O)$$

XII — IV and VI

$$CH_3\text{-}CH\text{-}CH\text{-}CH_2OCH_3 \xrightarrow{\oplus\ominus\ Na\ OCH_3} CH_3\text{-}CH(OH)\text{-}CH(OCH_3)\text{-}CH_2\text{-}OCH_3$$

IV — V and VII

The first plan adopted to prove the structures of IV and VI was to oxidize them with potassium permanganate solution and identify the acids formed. However, the yields

$$R\text{-}CH\text{-}CH\text{-}R' \xrightarrow{(O)} RCOOH + R'COOH$$

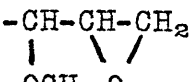
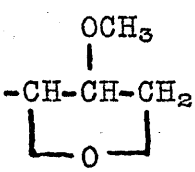
of these reactions were found to be very low and not enough material was obtained for identification purposes. Therefore, attention was turned to the other methods described below.

Products IV (67.4%, b.p. 121 - 122°)[a] and VI (42 - 54%, b.p. 122 - 124°) were shown by analyses to have the same empirical formula, $C_5H_{10}O_2$. Quantitative analyses for oxirane oxygen by the hydrogen chloride method of Swern[31] showed 96.3% of the theoretical oxirane oxygen in IV and 88.5 - 92.2% in VI. Analysis of IV by the periodate method gave 99.3%. These analyses stand as proof that the compounds were epoxides.

Both IV and VI, when treated with periodic acid gave the two aldehydes, acetaldehyde, X, and methoxyacetaldehyde, XI,

a. All temperatures recorded in this thesis are in degrees centigrade.

which were identified by mixed melting point measurements on the corresponding 2,4-dinitrophenylhydrazones. Since this reaction goes by hydrolysis of the epoxide to a glycol with subsequent cleavage of the glycol,[32] the compounds IV and VI must have had the structure as shown.

Of the other possible products listed on pages 9 and 11, the compound  would have given formaldehyde and alphamethoxypropionaldehyde and the compound  would not be cleaved by periodic acid because the first step would give a 1,3-glycol.[38]

Reduction with lithium aluminum hydride gave a known alcohol, 1-methoxy-2-butanol,[39] VIII (81.6% from IV and 81% from VI), which was identified by its boiling point, an elemental analysis, and mixed melting point measurements on its 3,5-dinitrobenzoate. An authentic sample of the alcohol was obtained by treating 1,2-epoxybutane with sodium methoxide which would be expected to give almost exclusively the secondary alcohol.[23]

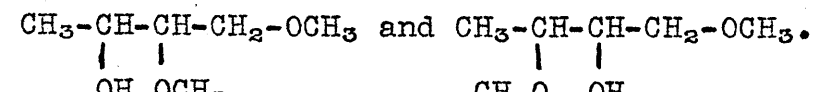
Catalytic reduction of IV yielded 61.4% of 1-methoxy-2-butanol, identified as described above, and also by chromic acid oxidation to the known ketone, 1-methoxy-2-butanone.[40,41] The ketone was identified by mixed melting point measurements on its 2,4-dinitrophylhydrazone. An authentic sample of the ketone was obtained by oxidation of a true sample of the alcohol.

Of all of the possible products listed on pages 9 and 11, E on page 9 and C on page 11, both of the same structure, $CH_3-CH-CH-CH_2-OCH_3$ (with an epoxide ring between the two CH groups), are the only ones which could give 1-methoxy-2-butanol by reduction. The compound $CH_3-CH(OCH_3)-CH-CH_2$ (with an epoxide ring between the CH and CH_2) would have given either 3-methoxy-2-butanol or 3-methoxy-1-butanol and the compound $CH_3-CH(OCH_3)-CH-CH_2$ (with an oxygen bridge between the CH and CH_2) would have given either 3-methoxy-2-butanol or 2-methoxy-1-butanol.

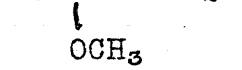
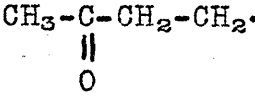
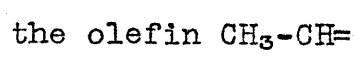
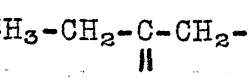
As further proof, the compound $CH_3-CH-CH-CH_2-OCH_3$ (with an epoxide ring between the two CH groups) was prepared by an independent method. Crotyl alcohol was treated with dimethyl sulfate to give methyl crotyl ether, XII, a known compound,[42] which was converted to a chlorohydrin by the well known chlorourea method.[43] The chlorohydrin was then converted to the epoxide by distillation from concentrated potassium hydroxide solution.[37,13] This methoxyepoxide also gave acetaldehyde and methoxyacetaldehyde when cleaved by periodic acid and was proved to be an epoxide by both the hydrogen chloride and periodate method.

Products V (5 - 16%, b.p. 168 - 170°) and VII (34%, b.p. 168 - 170°) were shown to be the same compound. Elemental analysis of V showed it to have the empirical formula, $C_6H_{14}O_3$ and a Zeisel determination showed the presence of two methoxy groups. Both V and VII gave positive iodoform tests, indicating

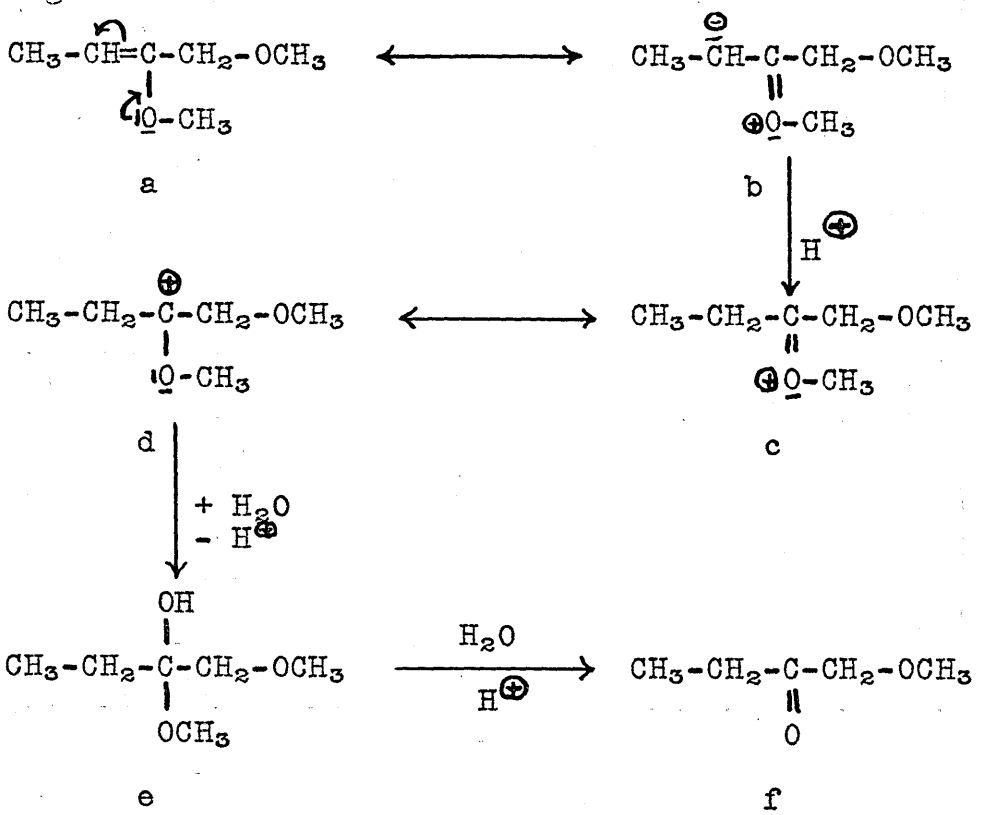
the presence of the CH_3-CHOH- function. Treatment of IV with sodium methoxide gave 80% of the product, b.p. 168 - 170°, showing that V and VII are the result of a secondary reaction. This limited the structure of the two to



A B

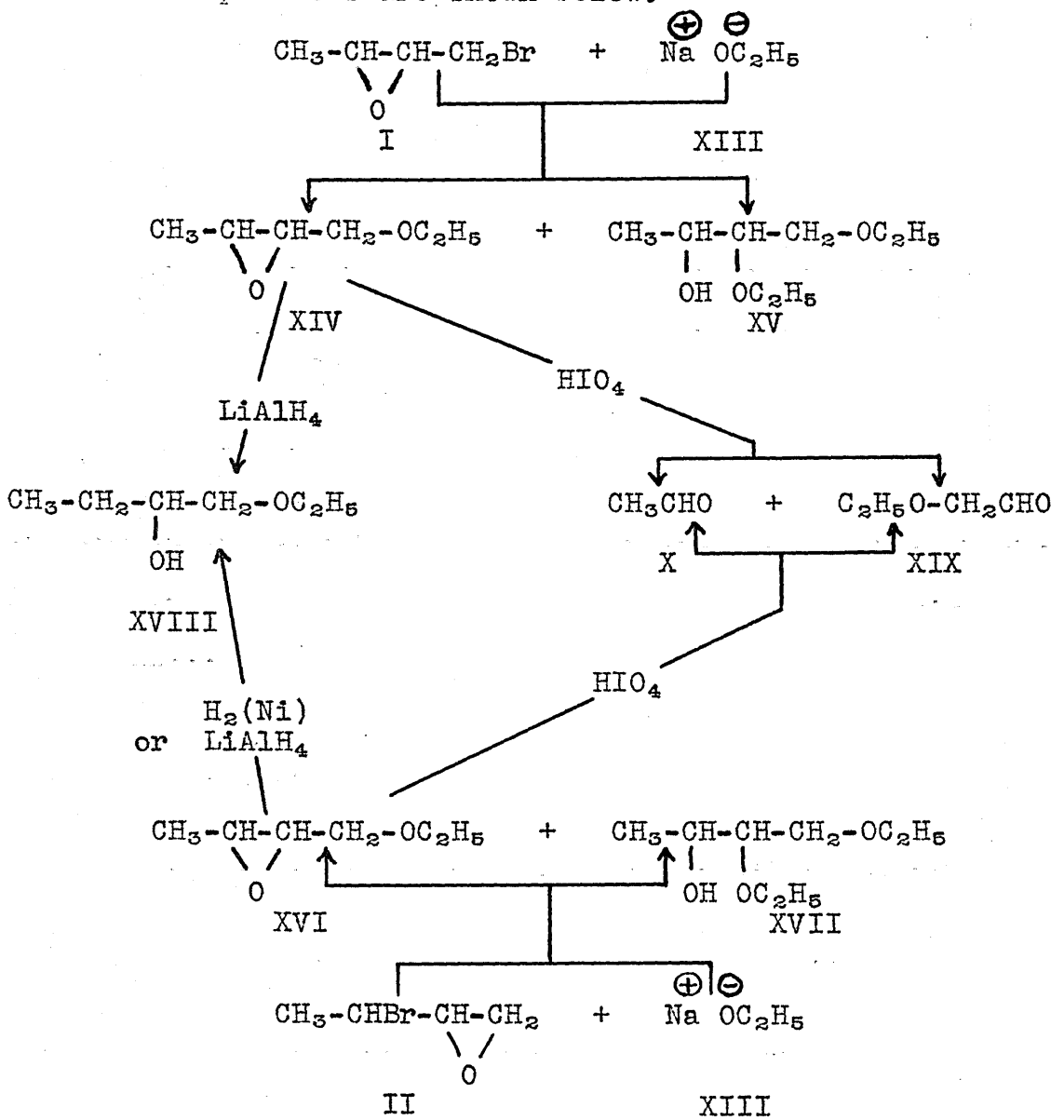
Treatment of V and VII with 50% sulfuric acid gave the ketone, 1-methoxy-2-butanone, IX, which was identified by a mixed melting point test and an analysis of its 2,4-dinitrophenylhydrazone. This ketone could have come only from structure A. Under the conditions of the experiment, the first step in the reaction would be expected to be dehydration to an olefin. Compound B, upon dehydration would give the olefin,  because, in such reactions, tertiary hydrogen atoms are lost much easier than secondary hydrogen atoms.[44] It has been shown by Hennion and coworkers[45] that this olefin, when treated with very dilute hydrochloric acid at room temperature, very rapidly rearranges to 4-methoxy-2-butanone,  . Compound A, however, would dehydrate to the olefin  [44] and by analogy to Hennion's results, would rearrange to 1-methoxy-2-butanone,  .

The following mechanism has been proposed for this rearrangement:



The olefin can be represented by another resonance form, b. Addition of a proton to b would give an ion which can be represented by the two resonance forms, c and d. The carbonium ion, d, is identical to the intermediate postulated in the hydrolysis of acetals and the mechanism from that point on is identical to that of the hydrolysis of acetals.[46]

The reactions of the two bromoepoxides with sodium ethoxide and the main reactions used in proving the structure of the products are shown below.



Products XIV (77.7%, 137.8 - 138.5°) and XVI (69.5 - 83.3%, b.p. 137 - 138°) were shown by analysis to have the empirical formula $C_6H_{12}O_2$. Compound XIV showed 95.6 - 98.4% of the theoretical oxirane oxygen by the hydrogen chloride method[31] and XVI showed 98.8 - 101.2% of the theoretical by the periodate method.

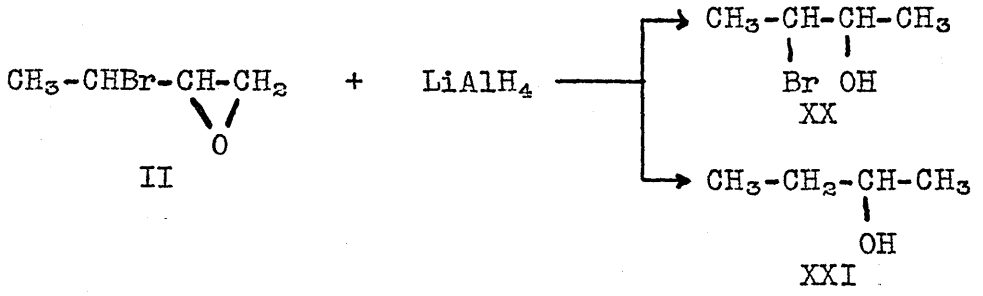
When treated with periodic acid, both XIV and XVI yielded the two aldehydes, acetaldehyde, X, and ethoxyacetaldehyde, XIX, which were identified by mixed melting point measurements on their 2,4-dinitrophenylhydrazones.

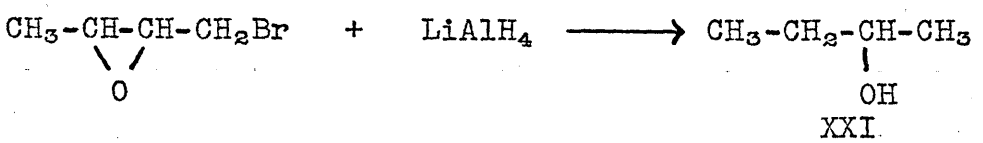
Reduction with lithium aluminum hydride gave 1-ethoxy-2-butanol, XVIII (65.4% from XIV and 59.3% from XVI), which was identified by comparison of the boiling point with an authentic sample and by oxidation with chromic acid to the known ketone, 1-ethoxy-2-butanone.[47,48] The ketone was identified by mixed melting point measurements on its 2,4-dinitrophenylhydrazone. An authentic sample of the ketone was obtained by oxidation of a true sample of the alcohol which was obtained by treating 1,2-epoxybutane with sodium ethoxide.[23]

Compound XVI was reduced catalytically to the same alcohol, XVIII (54%), which was identified as described above and by elemental analysis of the alcohol, as well as of the 2,4-dinitrophenylhydrazone derivative.

The structures of products XV (6.2%, b.p. 194 - 197°) and XVII (3.9%, b.p. 190 - 195°) have not been definitely established but they are both believed to be 3,4-diethoxy-2-butanol by analogy to the sodium methoxide reactions. An elemental analysis showed XV to have the expected empirical formula, $C_8H_{18}O_3$.

The two bromoepoxides were treated with lithium aluminum hydride and yielded the products as shown below:





From 3-bromo-1,2-epoxybutane, II, was obtained dl-threo-3-bromo-2-butanol, XX (51.4%, b.p. 50 - 51° at 14 mm.) and 2-butanol, XXI (24.1%). Both are known compounds.[49,50] The 2-butanol was identified by a mixed melting point measurement on its 3,5-dinitrobenzoate. The melting point of the 3,5-dinitrobenzoate of the dl-threo-3-bromo-2-butanol checked the value reported in the literature.[50] An elemental analysis showed the correct empirical formula, $C_{11}H_{11}N_2BrO_6$.

From 1-bromo-2,3-epoxybutane, I, only one product, 2-butanol (45.5%) was obtained. Starting material (41.7%) was recovered.

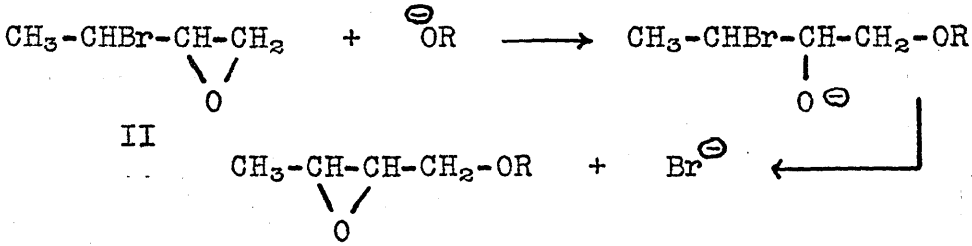
In these reactions only enough lithium aluminum hydride was used to reduce one function (e.g. epoxide or bromide).

Ten compounds were analyzed for oxirane oxygen by treatment with an excess of periodic acid and determination of the excess acid iodimetrically. The results of these runs are given briefly here.

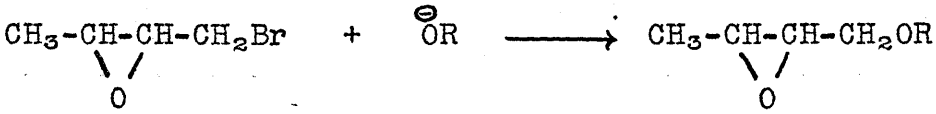
Compound	Ave. % of theoretical oxirane oxygen found
2,3-epoxybutane	99.8
1,2-epoxybutane	102.4
1-methoxy-2,3-epoxybutane	98.0
1-ethoxy-2,3-epoxybutane	100.0
1-bromo-2,3-epoxybutane	102.8
3-bromo-1,2-epoxybutane	98.4
cyclohexene oxide	99.2
styrene oxide	93.2
1,2-3,4-diepoxybutane	94.3
3,4-epoxy-1-butene	143.2

DISCUSSION OF RESULTS

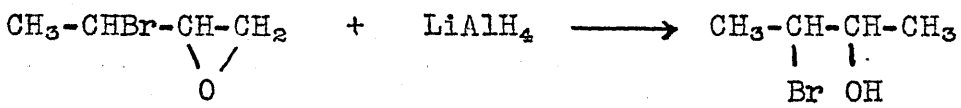
The results show that a neighboring group mechanism was operative in the reactions of 3-bromo-1,2-epoxybutane, II, with sodium methoxide, III, and with sodium ethoxide, XIII.



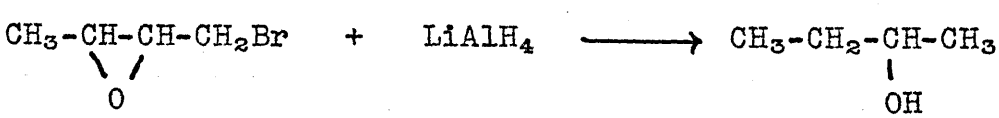
However, the reactions of 1-bromo-2,3-epoxybutane, I, with the same two bases proceeds by direct simple displacement of the bromide ion by alkoxide ion. The neighboring group



effect did not take place in the reaction of II with lithium aluminum hydride since the bromine was not displaced at all.



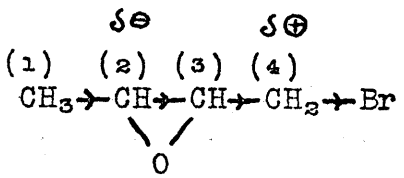
The results of the reaction of I with lithium aluminum hydride do not show which mechanism prevailed.



It is evident that both the epoxide group and the alkyl bromide are quite reactive toward the alkoxide ion. These

results do not show which is the more reactive, but show rather that the whole molecule must be taken into consideration in any prediction concerning the course of a reaction. In this competition between bromide and epoxide, the function which was on the end of the molecule was attacked first. This indicates that steric requirements might be the dominating directive force.

These results can also be explained by an electronic interpretation. A negatively charged base would be expected to attack at the most positive point of the molecule. In II, the most positive point in the molecule is the carbon atom

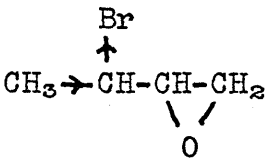


II

holding the bromine atom. The electronegative bromine atom would draw electrons to it, leaving carbon (4) slightly positive. This inductive effect is diminished as it is passed down a chain[51] and thus the displacement of electrons from carbon (3) toward carbon (4) would be slight. On the other end of the molecule, the electron-donating methyl group tends to make carbon (2) negative. This effect is also diminished as it is passed down the chain and the electron displacement from carbon (2) to carbon (3) would be slight. Carbon atom (3) has electrons shifted toward it from the left and away from it to the right. This would leave it practically

uncharged.

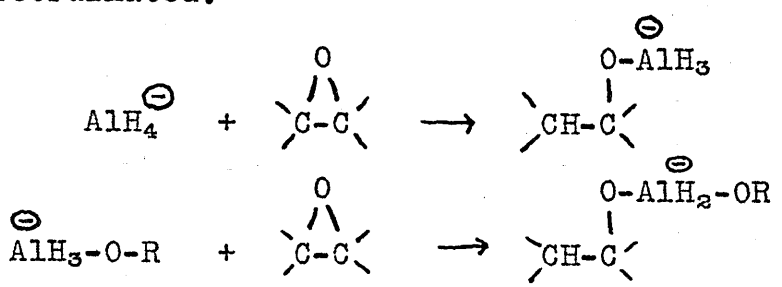
In compound I, the bromine atom and the methyl group



I

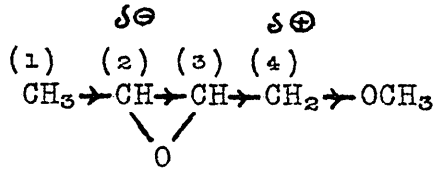
are both attached to the same carbon atom and their effects would tend to cancel each other. Thus, the three possible points of attack would be essentially uncharged, leaving steric effects to direct the attack alone. From this, a terminal attack would be expected, which was found to be the case.

The reason that a neighboring group effect does not take place in the reaction of the terminal epoxide, II, with lithium aluminum hydride is probably because of the presence of the aluminum atom. Trevoy and Brown[24] have postulated that the attacking group in lithium aluminum hydride reactions is a series of aluminohydride ions, $AlH_4^{\ominus}$, $AlH_3X^{\ominus}$, $AlH_2X_2^{\ominus}$ and $AlHX_3^{\ominus}$, where X denotes an alkoxide ion to which the aluminum atom is coordinated.



If an aluminum atom were coordinated with the epoxide oxygen at the time of the attack, it could prevent the second step of the reaction, the neighboring group effect, from taking place.

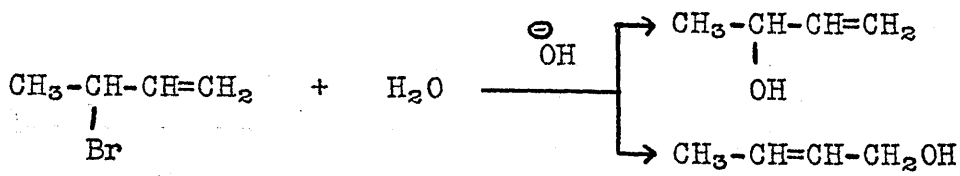
The reaction of the methoxy epoxide (IV and VI) with another mole of methoxide ion to give 3,4-dimethoxy-2-butanol can be explained easily by an electronic interpretation. This molecule is very similar electronically to the corr-



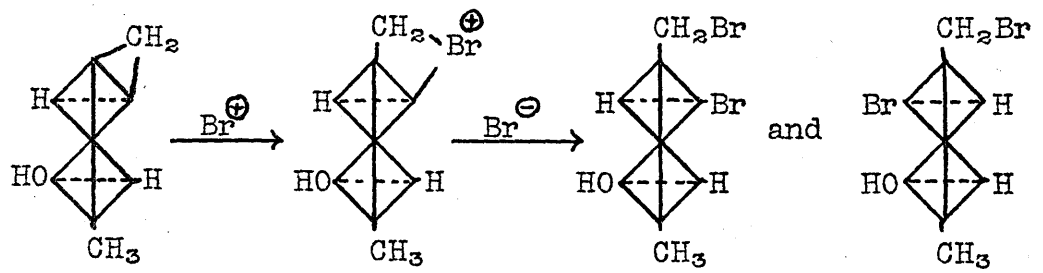
sponding bromoepoxide. Again carbon (2) would be the most negative and carbon (4) the most positive. The attack comes at carbon (3), probably, because that position, even though not positively charged, is less negative than carbon (2). Carbon atoms (2) and (3) are the only possible points of attack.

The methoxyepoxides IV and VI and also the ethoxyepoxides, XIV and XVI, which were proved to have the same carbon skeleton, may not be identical.

As will be pointed out later in this section, the 3-bromo-1,2-epoxybutane, II, was proved to be of the threo configuration. However, from the method of its preparation,[37] it must be assumed that the 1-bromo-2,3-epoxybutane, I, was a mixture of two pair of racemates. The methyl vinyl carbinol from which it was prepared was obtained by hydrolysis of crotyl bromide with dilute sodium carbonate solution.



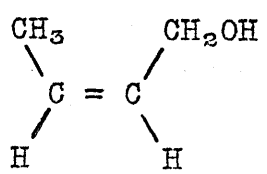
Under these conditions, the S_N1 or carbonium ion mechanism prevails.[9] Thus the methyl vinyl carbinol undoubtedly was a racemic mixture of two possible stereoisomers. The next step, addition of bromine to the double bond, would have given two sets of racemates by the accepted mechanism for this type of reaction.[13,14] The last step, which involves removal of a



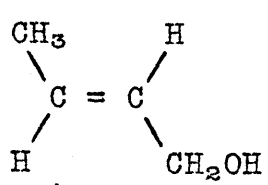
racemic pair racemic pair racemic pair

proton from the OH group, with subsequent intramolecular displacement of the neighboring bromine atom by the oxide ion,[13] would cause an inversion of the configuration of the carbon atom from which the bromine is displaced. Thus the bromoepoxide would consist of two pair of racemates which probably could not be separated by distillation.

The other bromoepoxide, II, was prepared by the same reactions starting with crotyl alcohol which was obtained along with the methyl vinyl carbinol by hydrolysis of crotyl bromide. Crotyl alcohol does not contain an asymmetric carbon atom as does its isomer but it can exist in cis and trans forms. When converted to the bromoepoxide, both the



cis

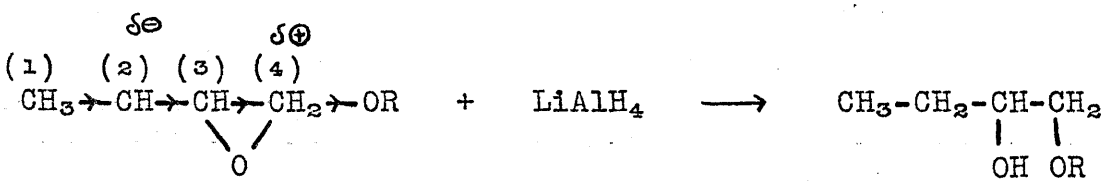


trans

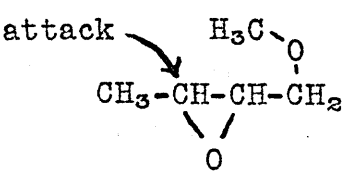
cis and trans would produce a pair of racemates. It has been shown, however, that only that pair which would be formed from the trans isomer was actually obtained.

When treated with sodium methoxide or sodium ethoxide, II, by the neighboring group mechanism, undergoes an inversion at the carbon atom from which the bromine is displaced. However, the final product is still of only one configuration. The products of I with alkoxides still would be two pair of racemates which probably would have very similar physical properties. This may be the reason that the boiling points and refractive indices of the alkoxyepoxides (IV and VI, XIV and XVI) did not check exactly.

The results of the reactions of lithium aluminum hydride seem to show that steric hindrance is more important than electronic effects in these reactions. In the reactions with the alkoxyepoxides, the attack was at carbon (2), the most



negative point in the molecule. This may have been caused by steric hindrance of the alkoxy group. The attacking group as postulated by Trevoy and Brown[24] is large and model studies show that a methoxy group is large enough to block an attack on an adjacent carbon atom if swung around to the correct

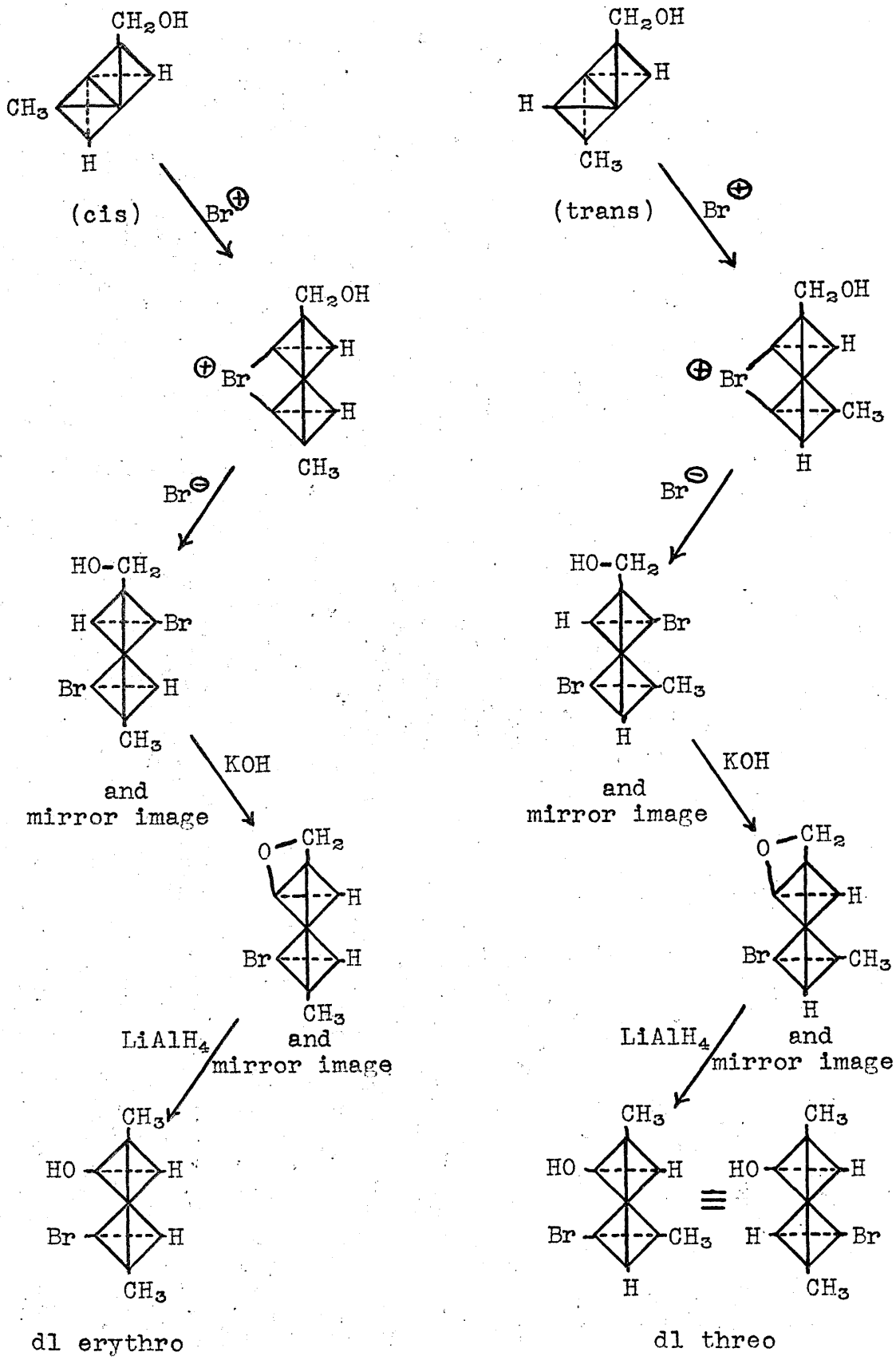


position. The work of Prins,[28] which was discussed in the introduction, shows that the methoxy group is effective in this role. However, since the methoxy group is free to rotate about a single bond, it is difficult to see why it should spend all of its time in the one particular position necessary to block this attack.

These results indicate that this attacking group is larger than the methoxide ion, since methoxide ion did attack at carbon (3).

In the reaction of II with lithium aluminum hydride, the terminal, less hindered carbon atom of the epoxide was attacked first. The bromine apparently was not displaced until all of the epoxide had reacted. This tends to substantiate the steric hindrance idea.

The fact that essentially pure dl-threo-3-bromo-2-butanol was obtained from this reaction is of great significance. Since there would be no change of configuration in going from the bromoepoxide to the bromohydrin (no bonds are broken at asymmetric carbon atoms), the bromoepoxide also must have been of the threo configuration. This means that the crotyl alcohol, from which the bromoepoxide was prepared, must have been the trans isomer. This is in agreement with Raman spectra data which shows that normal crotyl alcohol is at least 95% the trans isomer.[65] Cis crotyl alcohol would have given the erythro bromoepoxide and bromohydrin.


CH2OH
H
CH3
H
(cis)
Br⊕
CH2OH
⊕Br
H
H
CH3
Br⊖
HO-CH2
H
Br
Br
H
CH3
and
mirror image
KOH
O
CH2
H
Br
H
CH3
and
mirror image
LiAlH4
CH3
HO
H
Br
H
CH3
dl erythro
CH2OH
H
H
CH3
(trans)
Br⊕
CH2OH
⊕Br
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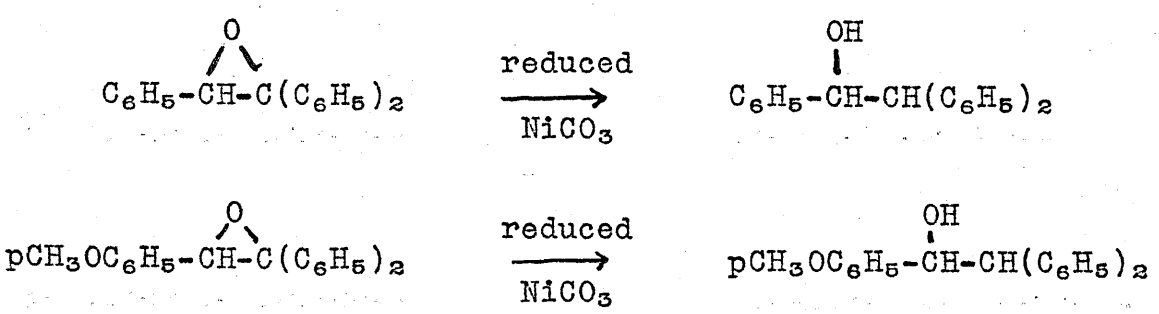
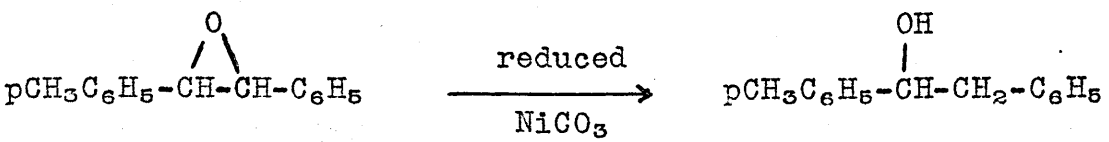
CH3
H
Br⊖
HO-CH2
H
Br
Br
CH3
H
and
mirror image
KOH
O
CH2
H
Br
CH3
H
and
mirror image
LiAlH4
CH3
HO
H
Br
CH3
H
≡
CH3
HO
H
H
Br
CH3
dl threo

Not much can be deduced from the results of the analogous reaction with I. Both the terminal bromide and the non-terminal epoxide were attacked and there is nothing to indicate which was attacked first.

Looking at both reactions together, it is quite clear that primary bromides are reduced easier than secondary bromides. This has been observed previously.[52]

Catalytic reduction of the alkoxy epoxides gave the same products as were obtained with lithium aluminum hydride. From these results and those reported in the literature for catalytic reduction of epoxides, no general deductions can be made. Newman[25] found that terminal epoxides, when reduced catalytically with Raney nickel, gave primary alcohols in neutral solutions but when traces of either acid or base were present, he obtained predominantly secondary alcohols. With lithium aluminum hydride he also obtained secondary alcohols. Grignard[53] states that catalytic hydrogenation of non-terminal epoxides produces alcohols in which the hydroxy function appears either on the least substituted or the most negative carbon atom. This is born out by three reactions reported by Weill and Kayser.[54]

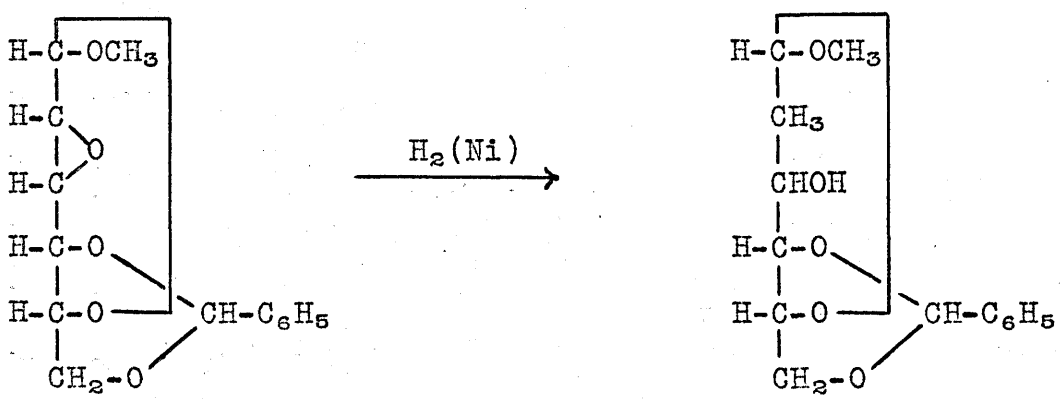




However, Plattner, Heusser and Feuer,[27] obtained a tertiary alcohol from the catalytic reduction of alpha-cholesterol acetate in which the epoxide lies between secondary and tertiary carbon atoms. In this case the results were the same as with lithium aluminum hydride (see page 15).

Weill and Kayser state that the rupture of the carbon-oxygen bridge is the opposite of that found on isomerization with heat and it may depend on the conditions under which the reduction is carried out and the nature of the catalyst.

Prins,[28] on reduction of the methyl-2,3 anhydropyranoside, as shown, obtained the 2-desoxy sugar (3-carbinol) no matter which side of the ring the epoxide function was on. Lithium aluminum hydride gave the 3-desoxy (2-carbinol) when the methoxy and epoxy groups were on opposite sides of the ring (see page 16).



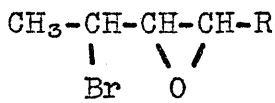
both cis and trans

The results of the oxirane oxygen determination with periodic acid are generally good. The extremely high results

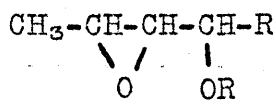
obtained with 3,4-epoxy-1-butene are probably due to the formation of the unsaturated aldehyde which may react further with periodic acid. The low results on styrene oxide are, however, better than those obtained by Swern[31] by the hydrogen chloride method. No reason can be offered for the low results on diepoxybutane. The average precision on two identical runs was about 2%. This method appears satisfactory for any epoxide which does not have other functions which will react with periodic acid. Some of these functions are 1,2 glycols, alphahydroxy aldehydes and ketones, 1,2-diketones and alpha-hydroxy acids.[3a] For water-insoluble compounds, dioxane solutions may be used.

SUGGESTIONS FOR FUTURE WORK

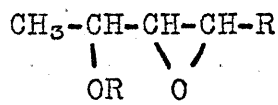
In order to shed more light on the relative reactivities of bromide and epoxide with basic reagents, reactions of bases with the following epoxide (R = ethyl or larger) should be run.



In this compound, all possible points of attack are secondary and thus the steric factors would be identical. Also, the two different mechanisms could be distinguished by the products obtained. A neighboring group mechanism would give



while a simple direct displacement would give



These products could be identified by the same methods used in the present work.

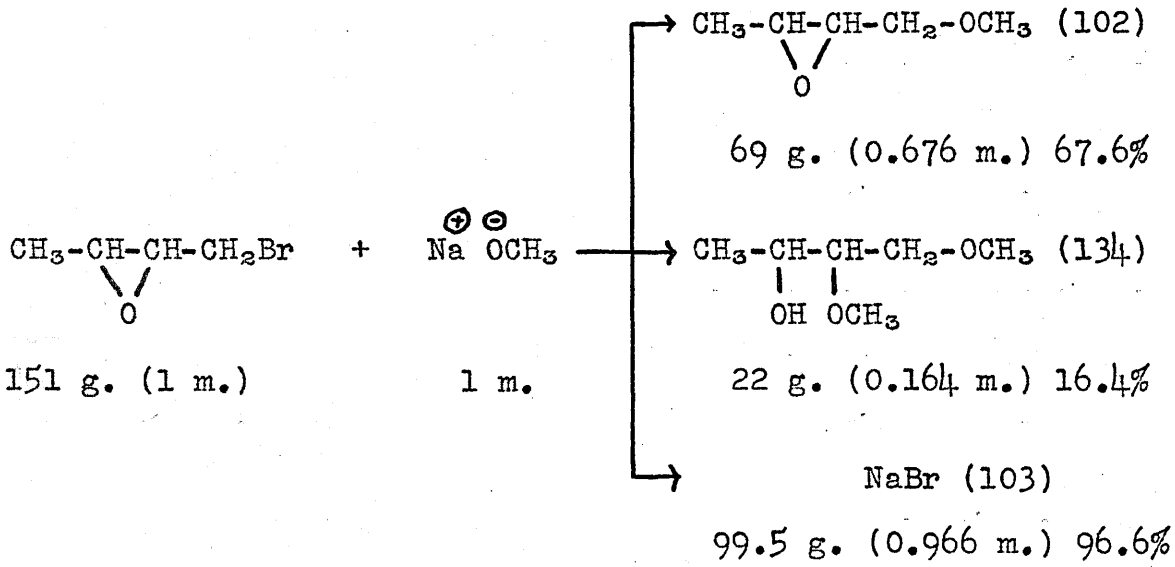
A method of preparing this type of compound is given by Helferich and Bester.[55] It consists of the addition of bromine to crotonaldehyde to give 2,3-dibromocrotonaldehyde, the condensation of the dibromoaldehyde with a Grignard reagent to give a dibromohydrin and distillation of the dibromohydrin from concentrated potassium hydroxide to produce the final alphabromoepoxide.

EXPERIMENTAL

PART I

The Reaction of 1-Bromo-2,3-epoxybutane with Sodium Methoxide and Reactions Used in Proving the Structure of the Products

Reaction of 1-Bromo-2,3-epoxybutane with Sodium Methoxide



To a stirred refluxing solution of 151 g. (1 mole) of 1-bromo-2,3-epoxybutane in 150 ml. of absolute methanol in a 500 ml. flask, a solution of 23 g. (1 mole) of sodium in 250 ml. of methanol was added over a 3 hr. period. Sodium bromide began to precipitate after 20 - 25 min. After 12 hr., most of the methanol was distilled off at atmospheric pressure. The remaining liquid was decanted from the solid sodium bromide, which was then extracted 3 times with 50 ml.

portions of absolute ether. The combined liquids were distilled at a reduced pressure giving two products, 69 g. (67.6%) of 1-methoxy-2,3-epoxybutane, b.p. 53.5 - 54.5° (55 mm.) and 121 - 122° (730 mm.), N_D^{10} 1.4096, N_D^{21} 1.4045, d_4^{21} 0.9410 and 22 g. (16.4%) of 3,4-dimethoxy-2-butanol, b.p. 93.5 - 94° (55 mm.) and 168 - 170° (730 mm.), N_D^{13} 1.4248, N_D^{24} 1.4204, d_4^{21} 0.9849 and 10 g. (6.7%) of the starting material, 1-bromo-2,3-epoxybutane. The yields, based on starting material not recovered, were 72.5 and 17.6% respectively. The sodium bromide, after an ether washing and drying, weighed 99.5 g. (96.6%). When an excess of sodium methoxide was used or when the solution was refluxed for a longer period of time, larger yields of the dimethoxy butanol were obtained.

Analysis of 1-methoxy-2,3-epoxybutane:

Calculated for $C_5H_{10}O_2$: C, 58.80; H, 9.80

Found: C, 58.68; H, 9.65

Analysis of 3,4-dimethoxy-2-butanol:

Calculated for $C_6H_{14}O_3$: C, 53.71; H, 10.44

Found: C, 53.67; H, 10.15

The higher boiling fraction, 3,4-dimethoxy-2-butanol, gave a positive iodoform test, indicating the presence of the CH_3-$\overset{|}{C}$OH- function and a Zeisel determination showed the presence of two methoxy groups.

Analysis: Calculated for 2 CH_3O groups: 46.3%

Found: 45.9%

The structures of these two products, were proved by the following reactions.

Determination of Oxirane Oxygen in 1-Methoxy-2,3-epoxybutane[a] (HCl Method)

$$CH_3\text{-}CH\text{-}CH\text{-}CH_2\text{-}OCH_3 \quad + \quad HCl \text{ (excess)} \longrightarrow \text{a chlorohydrin}$$
(the epoxide oxygen bridges the two CH groups)

This test was run according to the general method outlined by Swern.[31] It consists of treating the epoxide with an excess of anhydrous hydrogen chloride in ether and titrating the excess with standard sodium hydroxide. The percent of oxirane oxygen in the compound was calculated by the following equation:

$$\% \text{ oxirane oxygen} = \frac{B - (T - A) \times N \times 0.016 \times 100}{W}$$

where B = ml. of NaOH used in a blank run containing no epoxide.

T = ml. of NaOH used in back titration.

A = acid content of the sample expressed in ml. of NaOH required to neutralize the acid in W grams of sample.

N = normality of NaOH.

W = weight of sample in grams.

The sample of 1-methoxy-2,3-epoxybutane was weighed accurately into an erlenmeyer flask fitted with a light weight glass stopper, and 25 ml. of anhydrous hydrogen chloride in ether (0.2 - 0.3 N) was added by means of a pipette.

---

a. All of the 1-methoxy-2,3-epoxybutane and 3,4-dimethoxybutanol used in the reactions of PART I are the products of the first reaction described in this part. The organization of all other parts of this chapter is analagous.

After the stopper was wired in position, the flask was swirled a few times and allowed to stand 3 hr. Fifty ml. of 95% ethanol was added and the excess hydrogen chloride was titrated with standard sodium hydroxide rapidly to the first phenolphthalein end point. The acid content was determined by titrating a sample directly with sodium hydroxide.

N = 0.0963

W = 0.6991

A = negligible

B = 109.38

T = 40.52

% oxirane O = 15.11

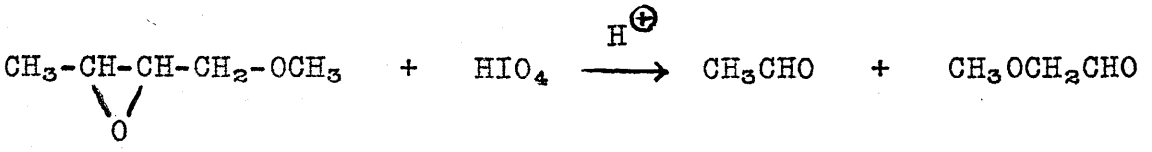
theoretical O = 15.7

% purity = 96.3

The oxirane oxygen content of this compound was also determined by the periodate method. The results and details of the method are given in a separate section.

Reaction of 1-Methoxy-2,3-epoxybutane

with Periodic Acid

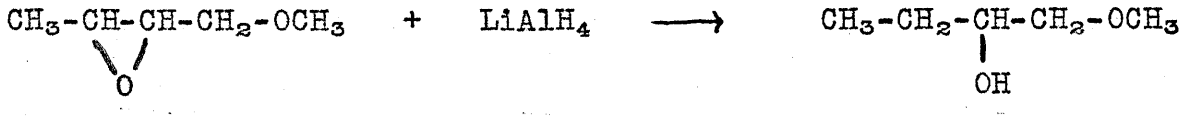


Two ml. of 1-methoxy-2,3-epoxybutane was added to a solution of 5 g. of paraperiodic acid (H_5IO_6) in 10 ml. of water containing 0.3 ml. of concentrated sulfuric acid, in a 50 ml. suction flask. The top of the suction flask was stoppered and a rubber tube was attached to the side arm. As the reaction proceeded the mixture became quite warm and acetaldehyde boiled off. The temperature was kept below 30° by cooling in a water bath. The acetaldehyde was passed into a solution of 2,4-dinitrophenylhydrazine prepared according to the method of Shriner and Fuson[56] and the yellow 2,4-dinitrophenylhydrazone formed was recrystallized 5 times from 75 - 80% ethanol. It melted at 164.5 - 166°. The melting point of a mixture of this and an authentic sample (m.p. 166 - 168°, accepted value, 168°[57]) was 164 - 166°.

When acetaldehyde no longer boiled off spontaneously, the suction flask was attached to an aspirator and as much as possible of the remaining acetaldehyde was removed by boiling the solution for 20 - 30 min. at 20° under 40 - 45 mm. pressure. To the remaining liquid was added a solution of 5 g. of silver nitrate in 5 ml. of water. The precipitated silver iodate and silver periodate were filtered off by suction. To remove the excess silver ion from solution, 1 g.

of sodium chloride was added and the precipitated silver chloride was filtered off. The solution was then mixed with a 2,4-dinitrophenylhydrazine solution[56] and the resulting precipitate was purified by recrystallizing from 75% ethanol. It yielded orange needles, m.p. 118.5 - 125°. The melting point of a mixture of this and an authentic sample (m.p. 123-125°, accepted value, 125°[58]) was 122.5 - 125°. The authentic sample of methoxyacetaldehyde was obtained by oxidation of methyl cellosolve with chromic acid.[59]

Reduction of 1-Methoxy-2,3-epoxybutane with Lithium Aluminum Hydride



(102)	(38)	(104)
30 g. (0.294 m.)	4 g. (0.105 m.)	25 g. (0.24 m.) 81.6%

A solution of 30 g. (0.294 mole) of 1-methoxy-2,3-epoxybutane in 50 ml. of absolute ether was added dropwise to a solution of 4 g. (0.105 mole) of lithium aluminum hydride in 50 ml. of ether in a 250 ml. erlenmeyer flask fitted with a magnetic stirrer, a reflux condenser and a dropping funnel. The solution refluxed vigorously during the addition (30 min.) and was kept at the boiling point for 3 hr. longer. At the end of this time, 20 ml. of water was added to hydrolyze the excess lithium aluminum hydride and the alcoholate formed in the reaction. This gave rise to a pasty mass assumed to be

aluminum hydroxide. The solid was filtered off and washed 3 times with 15 ml. portions of ether and the combined ether solutions were dried over magnesium sulfate and distilled at atmospheric pressure. The only product obtained was 25 g. (81.6%) of 1-methoxy-2-butanol, b.p. 134 - 135° (740 mm.), N_D^{23} 1.4115 (reported, b.p. 133 - 133.6°, N_D^{25} 1.4106).[39] In another reaction, in which the refluxing period was only 15 min., the yield was only 32%.

A 3,5-dinitrobenzoate (m.p. 85 - 88.3°) was prepared from the product and compared with the same derivative (m.p. 90 - 91°, reported, 91°[39]) made from an authentic sample of 1-methoxy-2-butanol obtained from the reaction of 1,2-epoxybutane with sodium methoxide. The melting point of a mixture of the two was 88.3 - 89.8°.

Analysis of 1-methoxy-2-butanol:

Calculated for $C_5H_{12}O_2$: C, 57.66; H, 11.61

Found: C, 57.84; H, 11.51

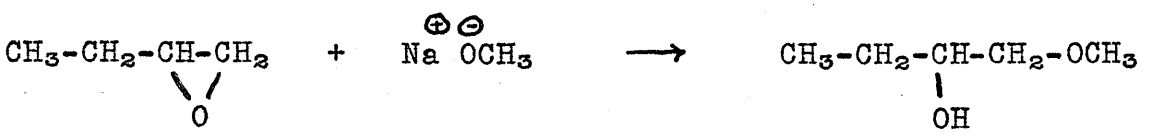
Analysis of the 3,5-dinitrobenzoate:

Calculated for $C_{12}H_{14}N_2O_7$: C, 48.32; H, 4.73; N, 9.39

Found: C, 48.53; H, 4.47; N, 9.15

Preparation of 1-Methoxy-2-butanol

from 1,2-Epoxybutane



(72) (104)

24.5 g. (0.34 m.) 0.35 m. 15 g. (0.144 m.) 42.5%

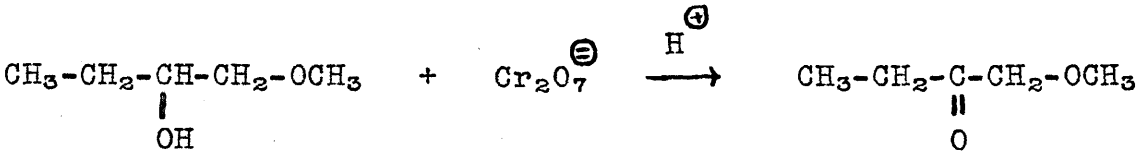
Sodium (8 g. or 0.35 mole) was dissolved in 100 ml. of absolute methanol and to this solution was added 24.5 g. (0.34 mole) of 1,2-epoxybutane. The mixture was refluxed for 8 hr. and allowed to stand for 48 hr. at room temperature. Water (20 ml.) was added to hydrolyze the alcoholate and the mixture was extracted 3 times with 100 ml. portions of ether. After a preliminary distillation at 200 mm. to remove any traces of sodium hydroxide, the solution was dried over anhydrous potassium carbonate and distilled at atmospheric pressure. The distillation yielded 6 g. of an azeotropic mixture of 1-methoxy-2-butanol and water, b.p. 93 - 94°, and 15 g. of pure product, b.p. 134.8 - 135.8° (740 mm.), N_D^{23} 1.4110 (reported, b.p. 133 - 133.6, N_D^{25} 1.4106).[39] A 3,5-dinitrobenzoate, m.p. 90 - 91° (reported, 91°)[39] was prepared.

Analysis of the 3,5-dinitrobenzoate:

Calculated for $C_{12}H_{14}N_2O_7$: C, 48.32; H, 4.73; N, 9.39

Found: C, 48.29; H, 4.69; N, 9.35

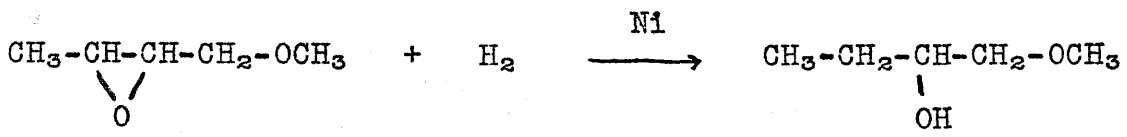
Preparation of 1-Methoxy-2-butanone



This reaction was run according to the general method outlined by Lucas and Pressman.[60]

Five grams (0.048 mole) of 1-methoxy-2-butanol, prepared from 1,2-epoxybutane, was added to a cooled solution of 6 ml. of concentrated sulfuric acid in 15 ml. of water. While the mixture was kept below 40° by cooling in a water bath, sodium dichromate (4.6 g. or 0.017 mole in 5 ml. of water) was added slowly. After all of the reagent was added, the mixture was allowed to stand until it attained the dark green color of chromic ion (about 10 min.), 10 ml. of water was added and the solution was distilled. An azeotropic mixture (5 - 6 g.) of 1-methoxy-2-butanone and water, b.p. 90 - 97° (reported, 90°),[40] was collected. From this was prepared a 2,4-dinitrophenlyhydrazone, m.p. 197 - 198° (reported, 198 - 198.5°).[42]

Catalytic Reduction of 1-Methoxy-2,3-epoxybutane



(102) (104)

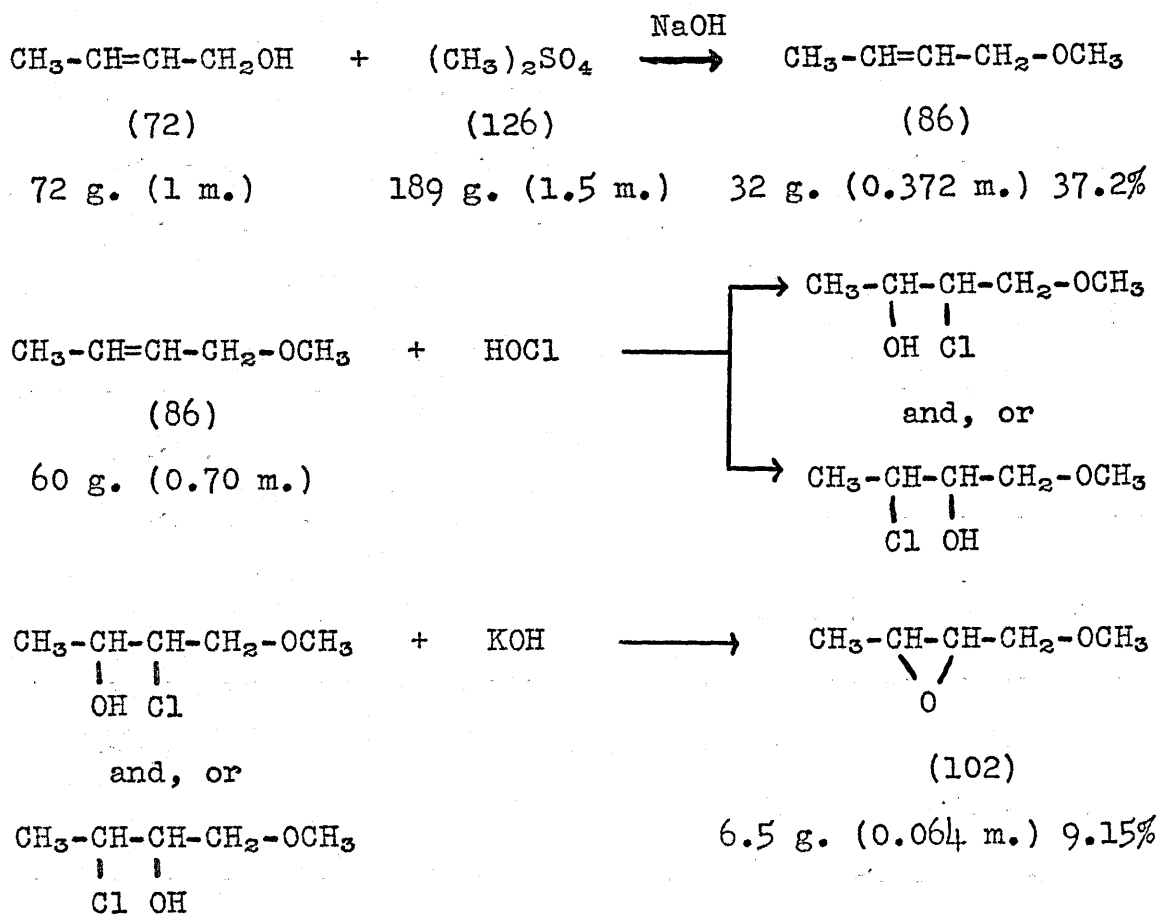
20 g. (0.196 m.) 12.5 g. (0.12 m.) 61.4%

Twenty grams (0.196 mole) of 1-methoxy-2,3-epoxybutane was dissolved in 50 ml. of absolute methanol, 2.5 g. of Raney nickel was added and the mixture was hydrogenated for a period of 3 hr. at 900 psig. and 130°. The catalyst was filtered off and the liquid distilled, giving 10 g. of only one major fraction, 1-methoxy-2-butanol, b.p. 134 - 136°, N_D^{20} 1.4123 (reported, b.p. 133 - 133.6°, N_D^{25} 1.4106).[39] Another fraction, (2.5 g.), b.p. 132.5 - 134°, N_D^{20} 1.4110, was essentially pure 1-methoxy-2-butanol. The two fractions together represented a yield of 61.4%. A 3,5-dinitrobenzoate was made of each fraction, and both melted at 89 - 90°. The melting point of a mixture of these and an authentic derivative (m.p. 90 - 91°) melted at 89 - 91° (reported, 91°).[39]

A 2.5 g. sample of the alcohol was oxidized to 1-methoxy-2-butanone exactly as described previously and a 2,4-dinitrophenylhydrazone (m.p. 197 - 198°, reported, 198 - 198.5[41]) was prepared. A mixed melting point determination with the authentic derivative (m.p. 197 - 198°) showed no depression.

Preparation of 1-Methoxy-2,3-epoxybutane

from Crotyl Alcohol



The first reaction was run according to the general procedure given by Hiers and Hager.[61] Seventy-two g. (1 mole) of crotyl alcohol was mixed with a cold solution of 80 g. (2 mole) of sodium hydroxide in 200 ml. of water in a 1 liter, 3-necked, round-bottom flask fitted with a stirrer, a thermometer extending into the liquid and a dropping funnel. The two-phased mixture was kept homogeneous by vigorous stirring at 15 - 25° by cooling in a water bath while 189 g. (1.5 mole) of dimethyl sulfate was added (2 hr.). Cooling and stirring were continued for 4 additional hours. After

this time, the top layer was taken off by means of a separatory funnel and dried for 12 hr. over potassium carbonate. Distillation gave 32 g. (0.372 mole) of methyl crotyl ether, b.p. 79° (reported, 79°),[42] and 20 g. of crotyl alcohol. The yield, based on crotyl alcohol not recovered, was 51.7%.

The addition of hypochlorous acid to this olefinic ether was carried out according to the general method described by Donahoe and Vander Werf.[43] Sixty g. (0.697 mole) of olefin and proportional quantities of urea, calcium carbonate, chlorine and water were used and the exact procedure was followed except that the final product was not purified. A mixture of two chlorohydrins was expected and since both would give the same epoxide, no attempt was made to separate them.

The formation of the epoxide was brought about by distilling the chlorohydrin from hot concentrated potassium hydroxide.[37] The crude chlorohydrin was added dropwise to a solution of 188 g. of potassium hydroxide in 50 ml. of water heated to 140 - 160° in a 500 ml. 3-necked round-bottom flask equipped with an efficient stirrer, a dropping funnel and a condenser set downward for distillation. The product distilled out as the chlorohydrin was added. It was dried for 12 hr. over potassium carbonate and distilled, yielding 30 g. (0.35 mole) of the olefin and 6.5 g. (0.064 mole) of 1-methoxy-2,3-epoxybutane, b.p. 121 - 122° (731 mm.), N_D^{23} 1.4053. The overall yield for the last two reactions, based on starting material not recovered was 18.3%.

Analysis of 1-methoxy-2,3-epoxybutane:

Calculated for $C_5H_{10}O_2$: C, 58.80; H, 9.87

Found: C, 58.52; H, 9.63

This epoxide was cleaved with periodic acid exactly as described previously. Acetaldehyde and methoxyacetaldehyde were isolated in the form of 2,4-dinitrophenylhydrazones (m.p. 164 - 166° and 120 - 124°). Mixed melting point measurements with authentic derivatives (m.p. 166 - 168° and 123 - 125°) showed no depression.

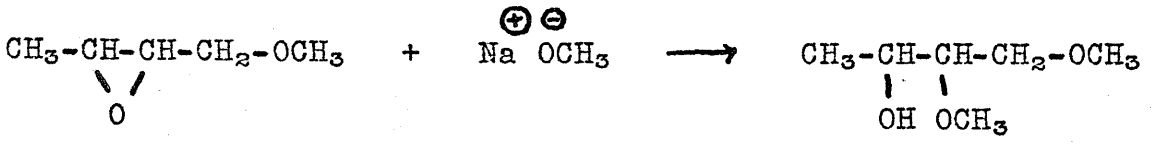
This product was analyzed for oxirane oxygen by the hydrogen chloride method as described on page 43 and by the periodate method, the results and description of which are given in a separate section.

Data for the hydrogen chloride method:

Sample	I	II
N	0.1203	0.1203
W	0.6320	0.6568
A	negligible	negligible
B	68.00	68.00
T	19.30	15.90
% oxirane O	15.15	15.23
theoretical	15.7	
% purity	96.0	97.0

Reaction of 1-Methoxy-2,3-epoxybutane

with Sodium Methoxide

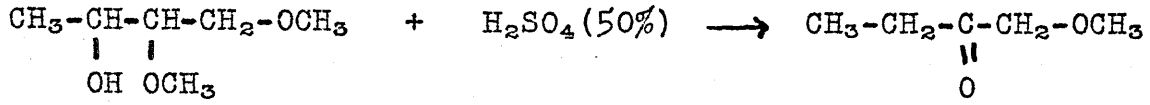


(102)		(134)
20 g. (0.196 m.)	0.2 m.	21 g. (0.157 m.) 80%

Sodium (4.6 g. or 0.2 mole) was dissolved in 100 ml. of absolute methanol and to this solution was added 20 g. (0.196 mole) of 1-methoxy-2,3-epoxybutane. The mixture was refluxed for 4 hr. and allowed to stand without heating for an additional 18 hr. Water (15 ml.) was added to hydrolyze the alcoholate and the mixture was extracted 5 times with 50 ml. portions of ether. The mixture was distilled from an ordinary distilling flask at 210 mm. into a receiver cooled in dry ice and after drying 4 hr. over anhydrous potassium carbonate, it was distilled again at 55 mm. giving 21 g. (80%) of 3,4-dimethoxy-2-butanol, b.p. 93 - 94° (55 mm.), N_D^{24} 1.4208.

Formation of 1-Methoxy-2-butanone

from 3,4-Dimethoxy-2-butanol



Ten g. of 3,4-dimethoxy-2-butanol and 10 ml. of 50% sulfuric acid were placed in a 100 ml. flask and distilled. By the time 10 ml. of liquid had distilled, the material in the stillpot was completely charred and distillation was stopped. The distillate was dried over potassium carbonate and redistilled at 745 mm., yielding 1.5 ml. of methanol, b.p. 63 - 65°, and 1.5 ml. of an azeotropic mixture of water and 1-methoxy-2-butanone, b.p. 85 - 90° (reported, 90°).[40]

The higher boiling fraction reduced Tollens' reagent to give a good silver mirror. This phenomenon has been reported for several ketones of the type $CH_3O-CH_2-\overset{\overset{O}{\|}}{C}-R$, where R is an alkyl group.[62] A 2,4-dinitrophenylhydrazone was prepared which, after 1 crystallization from an ethanol-ethyl acetate mixture, melted at 197.5 - 198.5° (reported for 1-methoxy-2-butanone, 198 - 198.5).[41] The melting point of a mixture of this and the true derivative (m.p. 197 - 198°) melted at 197 - 198°.

Analysis of the 2,4-dinitrophenylhydrazone:

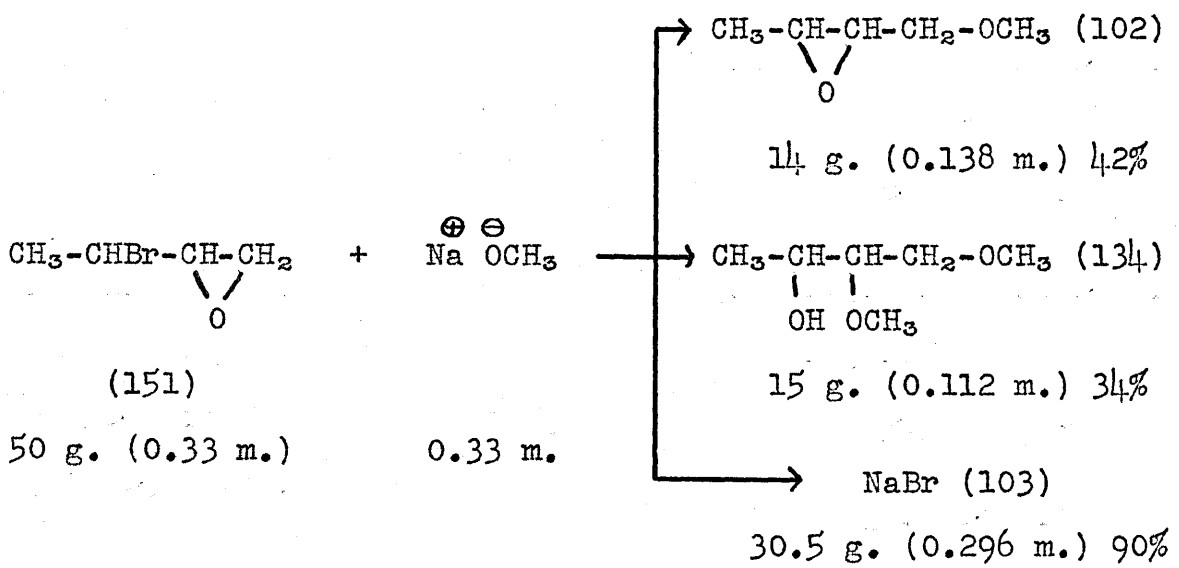
Calculated for $C_{11}H_{14}N_4O_5$: C, 46.81; H, 5.00; N, 19.86

Found: C, 46.74; H, 5.07; N, 19.21

PART II[a]

The Reaction of 3-Bromo-1,2-epoxybutane with Sodium Methoxide and Reactions Used in Proving the Structure of the Products

Reaction of 3-Bromo-1,2-epoxybutane with Sodium Methoxide



Distillation yielded 14 g. (42%) of 1-methoxy-2,3-epoxybutane, b.p. 53° (50 mm.), and 122 - 124° (745 mm.), N_D^{13} 1.4107, $N_D^{21.5}$ 1.4077, and 15 g. (34%) of 3,4-dimethoxy-2-butanol, b.p. 90 - 94° (50 mm.) and 165 - 170° (730 mm.), N_D^{24} 1.4214.

Another reaction gave 54% of the first product. The higher boiling fraction was lost.

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a. The reactions in the rest of this section, which are not given in detail here, were run in exactly the same manner as the analogous reactions in PART I.

Analysis of 1-methoxy-2,3-epoxybutane:

Calculated for $C_5H_{10}O_2$: C, 58.80; H, 9.87;

Found: C, 58.27; H, 9.73;

C, 58.50; H, 9.69;

The 3,4-dimethoxy-2-butanol gave a positive iodoform test and, when distilled from a 50% sulfuric acid mixture, gave 1-methoxy-2-butanone which formed a 2,4-dinitrophenylhydrazone (m.p. 197 - 198°, reported, 198 - 198.5°)[41] A mixture of this and a true derivative (m.p. 197.5 - 198.5°) melted at 197 - 198°.

Oxirane Oxygen Test on 1-Methoxy-2,3-epoxybutane

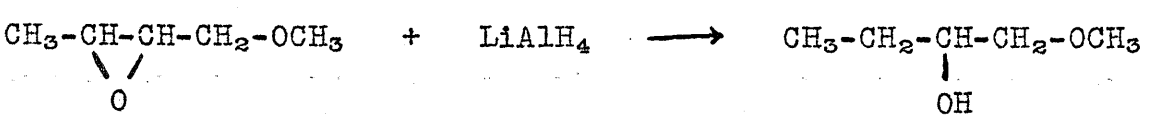
(HCl Method)

Sample	I	II
N	0.1203	0.1203
W	0.9942	0.9214
A	negligible	negligible
B	71.97	71.97
T	0.50	3.00
% oxirane O	13.84	14.41
theoretical	15.67	
% purity	88.5	92.2

Reaction of 1-Methoxy-2,3-epoxybutane with Periodic Acid

The two aldehydes, acetaldehyde and methoxyacetaldehyde were isolated in the form of 2,4-dinitrophenylhydrazones as before. The acetaldehyde derivative melted at 163 - 166°, an authentic derivative at 166 - 168° and a mixture of the two at 163.5 - 167°. The methoxyacetaldehyde derivative melted at 117 - 124°, an authentic derivative at 123 - 125° and a mixture of the two at 122 - 124°.

Reduction of 1-Methoxy-2,3-epoxybutane with Lithium Aluminum Hydride



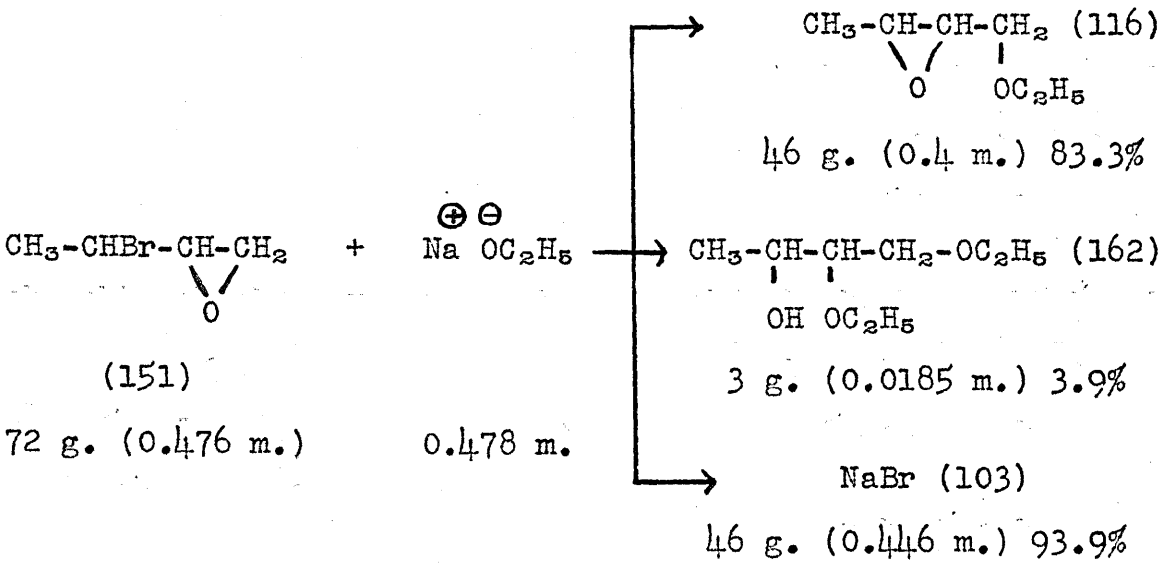
(102)	(38)	(104)
4.5 g. (0.044 m.)	2 g. (0.053 m.)	3.7 g. (0.035 m.) 81%

The epoxide (4.5 g. or 0.044 mole) was added dropwise to a solution of 2 g. of lithium aluminum hydride in 12 ml. of ether and the mixture was refluxed for 1 hr. After hydrolysis and drying, as before, the ethereal solution was distilled through a semimicro column, yielding 3.7 g. (81%) of one main fraction, 1-methoxy-2-butanol, b.p. 139°, N_D^{22} 1.4125 (reported, b.p. 133 - 133.6°, N_D^{25} 1.4106).[39] A 3,5-dinitrobenzoate (m.p. 89 - 90°, reported, 91°[39]) was prepared and a mixed melting point determination with an authentic sample showed no depression.

PART III

The Reaction of 3-Bromo-1,2-epoxybutane with Sodium Ethoxide and Reactions Used in Proving the Structure of the Products

Reaction of 3-Bromo-1,2-epoxybutane with Sodium Ethoxide



This reaction was run in exactly the same manner as the analogous reaction with sodium methoxide except that the time of addition and refluxing amounted to only 30 min. Distillation gave 46 g. (83.3%) of a main product, 1-ethoxy-2,3-epoxybutane, b.p. 76° (80 mm.) and 137 - 138° (731 mm.), N_D^{25} 1.4100 and 3 g. (3.9%) of a minor product believed to be 3,4-diethoxy-2-butanol, b.p. 190 - 195° (727 mm.), N_D^{20} 1.4302.

Analysis of 1-ethoxy-2,3-epoxybutane:

Calculated for $C_6H_{12}O_2$: C, 62.04; H, 10.41

Found: C, 61.69; H, 10.14

The results of an oxirane oxygen determination on 1-

ethoxy-2,3-epoxybutane by the periodate method are given in PART VI of this section.

Reaction of 1-Ethoxy-2,3-epoxybutane with Periodic Acid

This epoxide was treated with periodic acid under the same conditions described for 1-methoxy-2,3-epoxybutane and two aldehydes, acetaldehyde and ethoxyacetaldehyde were isolated in the form of 2,4-dinitrophenylhydrazones. The acetaldehyde derivative melted at 165 - 167°, an authentic sample at 166 - 168° and a mixture of the two at 165 - 167°. The ethoxyacetaldehyde derivative melted at 116 - 117° (reported, 116 - 117°).[58] An authentic sample and a mixture of the two also melted at this temperature.

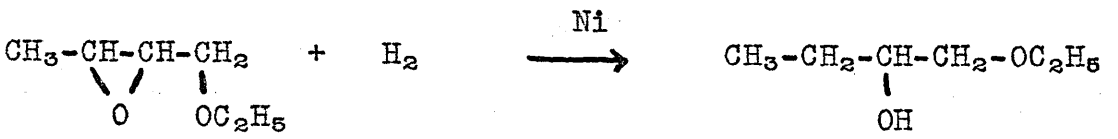
Analysis of the 2,4-dinitrophenylhydrazone of ethoxyacetaldehyde:

Calculated for $C_{10}H_{12}N_4O_5$: C, 44.78; H, 4.51; N, 20.90

Found: C, 44.92; H, 4.44; N, 21.20

The authentic sample of ethoxyacetaldehyde was obtained by oxidation of ethyl cellosolve.[59]

Catalytic Reduction of 1-Ethoxy-2,3-epoxybutane



(116) (118)

20 g. (0.172 m.) 11 g. (0.093 m.) 54%

Twenty g. of 1-ethoxy-2,3-epoxybutane and 2.5 g. of Raney nickel catalyst were mixed with 75 ml. of absolute methanol and placed in a high pressure hydrogenator. During 2 hr. at 500 psig., 1 hr. at 850 psig. and 1 hr. at 1200 psig. at 30°, no appreciable absorption of hydrogen was observed. Heat was then applied and the mixture was hydrogenated for 3 hr. while the pressure rose to 1500 psig. and the temperature rose to 170°. Subsequent cooling of the mixture brought about a considerable pressure drop, indicating that reduction had taken place. The catalyst was filtered off and the liquid distilled, giving 11g. (54%) of 1-ethoxy-2-butanol, b.p. 145 - 147° (740 mm.), N_D^{20} 1.4135 (authentic sample, b.p. 145 - 147° at 740 mm., N_D^{20} 1.4135). An attempt to prepare a 3,5-dinitrobenzoate of this product gave an oil which solidified at 0 - 10°.

Analysis of 1-ethoxy-2-butanol:

Calculated for $C_6H_{14}O_2$: C, 61.00; H, 11.87

Found: C, 61.22; H, 12.21

This alcohol was identified by oxidation to the corresponding ketone with chromic acid. Three ml. of the ethoxybutanol gave about 5 ml. of an azeotropic mixture of the

ketone and water (b.p. 94°). Separation of the two immiscible layers and drying the top layer over potassium carbonate, gave 1.5 ml. of 1-ethoxy-2-butanone, b.p. 140 - 147° (reported, 146 - 147°).[48] A 2,4-dinitrophenylhydrazone melted at 144 - 146° (reported, 146°)[47] and a mixture of this and an authentic sample (m.p. 144 - 146°) also melted at 144 - 146°.

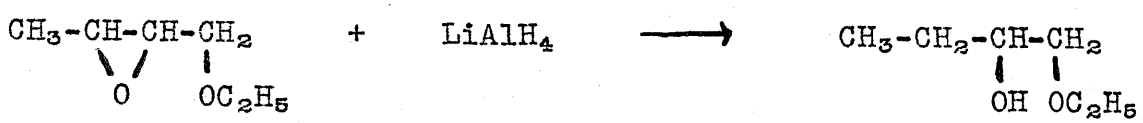
Analysis of the 2,4-dinitrophenylhydrazone of 1-ethoxy-2-butanone:

Calculated for $C_{12}H_{18}N_4O_5$: C, 48.64; H, 5.44; N, 18.91

Found: C, 48.80; H, 5.33; N, 19.10

The authentic sample of 1-ethoxy-2-butanol was obtained by treating 1,2-epoxybutane with sodium ethoxide according to the procedure outlined previously for the analogous reaction with sodium methoxide. Beginning with 10 g. (0.122 mole) of epoxide, a yield of 10 g. (69.5%) of 1-ethoxy-2-butanol (b.p. 145 - 147° at 740 mm., N_D^{20} 1.4135) was obtained. A small sample of this (2.5 g.) was oxidized with chromic acid to the ketone, 1-ethoxy-2-butanone, b.p. of azeotropic mixture, 94°, m.p. of 2,4-dinitrophenylhydrazone, 144 - 146° (reported, 146°).[47]

Reduction of 1-Ethoxy-2,3-epoxybutane with Lithium Aluminum Hydride



(116)	(38)	(118)
10 g. (0.086 m.)	2 g. (0.0526 m.)	6 g. (0.051 m.) 59.3%

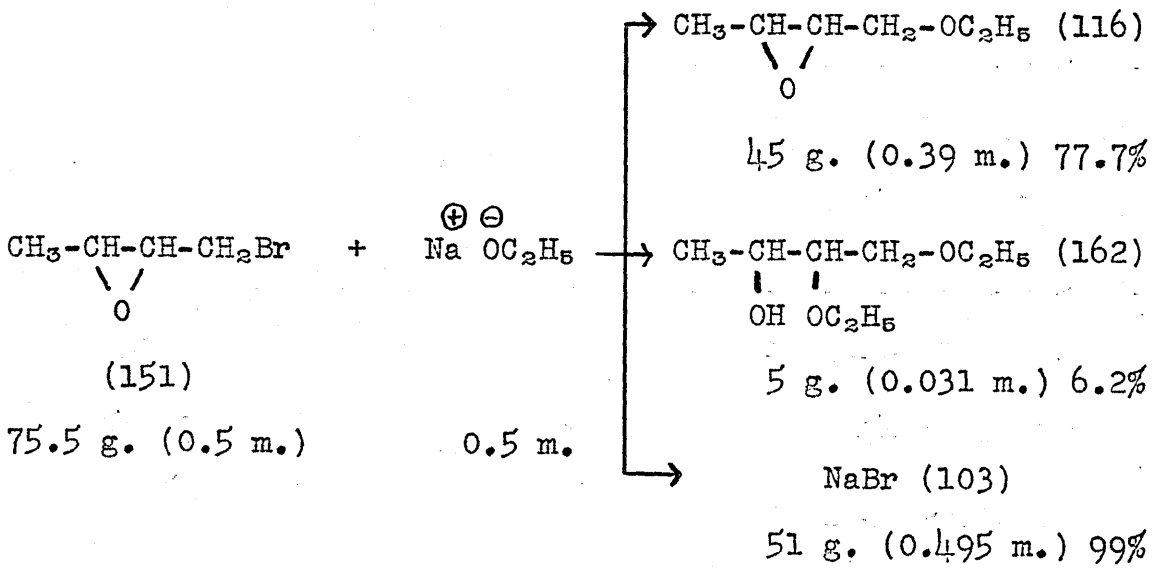
The reaction was run in the same manner as the analogous reaction with 1-methoxy-2,3-epoxybutane. Distillation gave 6 g. (59.3%) of one major fraction, 1-ethoxy-2-butanol, b.p. 145 - 147°, N_D^{20} 1.4135 (authentic sample, b.p. 145 - 147° at 740 mm., N_D^{20} 1.4135).

Three ml. of this compound was oxidized to the corresponding ketone with chromic acid. Distillation gave about 4 ml. of an azeotropic mixture of the ketone and water (b.p. 94°) which separated into 2 layers. From this was prepared a 2,4-dinitrophenylhydrazone, m.p. 144 - 146° (reported, 146°).[47] A mixture of this and an authentic sample (m.p. 144-146°) also melted at 144 - 146°.

PART IV

The Reaction of 1-Bromo-2,3-epoxybutane with Sodium Ethoxide and Reactions Used in Proving the Structure of the Products

Reaction of 1-Bromo-2,3-epoxybutane with Sodium Ethoxide



This reaction was run in exactly the same manner as the analogous reaction with sodium methoxide except that the addition and refluxing period amounted to only 30 - 40 min. The solvent, ethanol, was taken off at reduced pressure because excessive heating caused it to react further to give larger yields of the minor product and correspondingly smaller yields of the major product. Distillation of the products at atmospheric pressure gave 45 g. (77.7%) of 1-ethoxy-2,3-epoxybutane, b.p. 137.8 - 138.5° (747 mm.), N_D^{23} 1.4073 and 5 g. (6.2%) of 3,4-diethoxy-2-butanol, b.p. 194 - 197° (747 mm.), N_D^{24} 1.4248.

Analysis of 1-ethoxy-2,3-epoxybutane:

Calculated for $C_6H_{12}O_2$: C, 62.04; H, 10.41

Found: C, 62.27; H, 10.37

Analysis of 3,4-diethoxy-2-butanol:

Calculated for $C_8H_{18}O_3$: C, 59.23; H, 11.19

Found: C, 58.97; H, 10.90

Oxirane Oxygen Determination
on 1-Ethoxy-2,3-epoxybutane

Sample	I	II
N	0.1203	0.1203
W	0.6088	0.6546
A	negligible	negligible
B	68.02	68.02
T	26.72	22.00
% oxirane O	13.17	13.53
theoretical	13.77	13.77
% purity	95.6%	98.4%

Reaction of 1-Ethoxy-2,3-epoxybutane
with Periodic Acid

As in PART III, the two aldehydes, acetaldehyde and ethoxyacetaldehyde, were isolated in the form 2,4-dinitrophenylhydrazones. The acetaldehyde derivative melted at 164 - 166.5°, an authentic sample at 166 - 168° and a mixture

of the two at 164 - 166.5°. The ethoxyacetaldehyde derivative melted at 116 - 117° (reported, 116 - 117°).[58] An authentic sample and a mixture of the two also melted at this temperature.

Reduction of 1-Ethoxy-2,3-epoxybutane with Lithium Aluminum Hydride

(116)	(38)	(118)
9 g. (0.078 m.)	3 g. (0.079 m.)	6 g. (0.051 m.) 65.4%

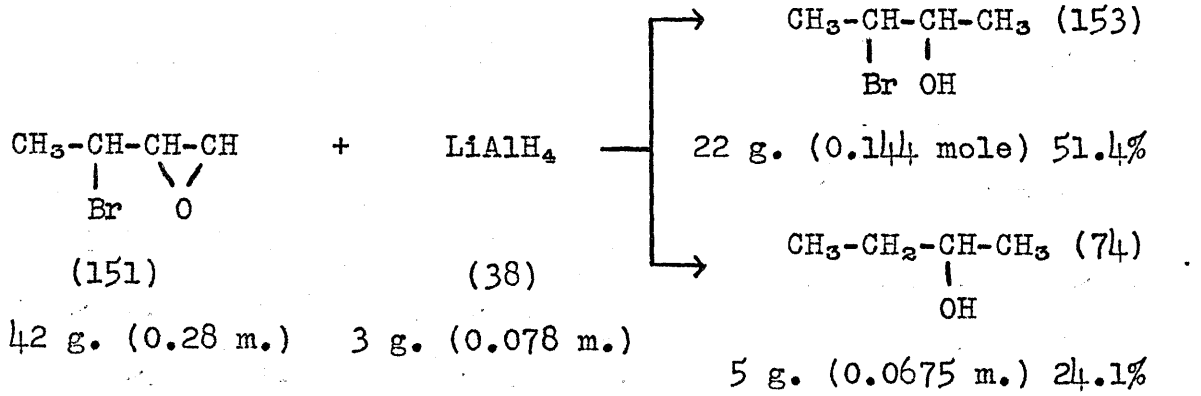
Carried out as described previously, the reaction yielded 6 g. (65.4%) of one product, 1-ethoxy-2-butanol, b.p. 145 - 147°, N_D^{20} 1.4135. A 2 g. sample was oxidized with chromic acid to give 1-ethoxy-2-butanone whose 2,4-dinitrophenylhydrazone melted at 144.5 - 146° (reported, 146°).[47] An authentic derivative and a mixture of the two both melted at 144 - 146°.

PART V

The Reaction of the Bromoepoxides

with Lithium Aluminum Hydride

3-Bromo-1,2-epoxybutane



To a solution of 3 g. (0.078 mole) of lithium aluminum hydride in 30 ml. of ether in a 200 ml. erlenmeyer flask fitted with a magnetic stirrer, a reflux condenser and a dropping funnel was added, dropwise, a solution of 42 g. (0.28 mole) of 3-bromo-1,2-epoxybutane in 30 ml. of absolute ether. The mixture refluxed vigorously as each drop was added. About 30 min. were required for the addition, after which the solution was refluxed for 2 hr. A small amount of white precipitate formed. After the refluxing period, the mixture was cooled in an ice bath and 30 ml. of water were added. A pasty solid, which was believed to be aluminum hydroxide, formed. The ether solution was decanted and the pasty mass was extracted 3 times with 20 - 25 ml. portions of ether. After drying for 12 hr. over anhydrous magnesium sulfate, the combined ether solutions were distilled under reduced pressure.

The ether was collected in a dry ice trap and redistilled later to check for the presence of volatile products, none of which were found. Distillation of the higher boiling material gave 5 g. (24%) of 2-butanol, b.p. 50 - 55° (100 mm.), N_D^{26} 1.3915 (reported, b.p. 99.5° at 760 mm., N_D^{25} 1.3949),[49] 17 g. (39.7%) of dl-threo-3-bromo-2-butanol, b.p. 50 - 51° (14 mm.), N_D^{26} 1.4750 (reported, b.p. 50.5° at 13 mm., N_D^{25} 1.4756)[50] and 5 g. (11.7%) of a fraction, b.p. 47 - 50° (14 mm.), N_D^{26} 1.4735, which was essentially dl-threo-3-bromo-2-butanol.

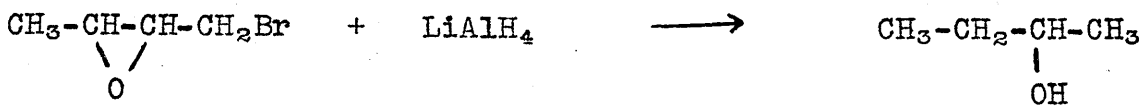
Solid 3,5-dinitrobenzoates were prepared from all three fractions. That from the 2-butanol melted at 75° (reported, 75°)[49] and the melting point of a mixture of this and an authentic sample (m.p. 75°) also melted at 75°. The derivatives of the last two fractions melted at 108 - 109° (reported, 109°)[50] and the melting point of a mixture of the two melted at 108 - 109°.

Analysis of the 3,5-dinitrobenzoate of dl-threo-3-bromo-2-butanol:

Calculated for $C_{11}H_{11}N_2BrO_6$:	C,	38.06;	H,	3.19
	N,	8.07;	Br,	23.02
Found:	C,	38.30;	H,	3.31
	N,	8.00;	Br,	22.8

The properties of dl-erythro-3-bromo-2-butanol are: b.p. 53.1° (13 mm.), N_D^{25} 1.4767, m.p. of the 3,5-dinitrobenzoate, 85°.[50]

1-Bromo-2,3-epoxybutane



(151)	(38)	(74)
36 g. (0.238 m.)	2.5 g. (0.066 m.)	8 g. (0.108 m.) 45.5%

Thirty-six g. (0.238 mole) of 1-bromo-2,3-epoxybutane was added dropwise to a stirred refluxing solution of 2.5 g. of lithium aluminum hydride in 50 ml. of absolute ether. At first the mixture refluxed vigorously when each drop was added but during the last half of the addition, no reaction appeared to take place. After the mixture had refluxed for 3 hr., it was cooled to 0° in an ice bath and 25 ml. of water was added. The pasty solid material was filtered off and washed 3 times with 25 ml. portions of ether. The combined ether solutions were dried for 6 hr. over anhydrous magnesium sulfate and distilled at a pressure of 14 mm.

All of the volatile products were collected in a dry ice trap. The only fraction collected was 15 g. (41.7%) of starting material, 1-bromo-2,3-epoxybutane, b.p. 40 - 41° (14 mm.), $N_D^{15.6}$ 1.4730 (reported, b.p. 54.5 - 55° at 25 mm., N_D^{15} 1.4736).[37]

The material collected in the dry ice trap was dried again over magnesium sulfate (12 hr.) and distilled at atmospheric pressure. It yielded 8 g. (45.5%) of 2-butanol, b.p. 95 - 100° at 742 mm. (reported, 99.5° at 760 mm.).[49] A 3,5-dinitrobenzoate (m.p. 75°, reported, 75°[49]) was prepared. A mixture of this and an authentic sample (m.p. 75°) also

melted at 75°.

The recovered 1-bromo-2,3-epoxybutane was analysed for oxirane oxygen content by the periodate method.

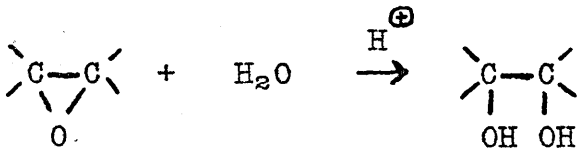
% oxirane oxygen found: 10.25

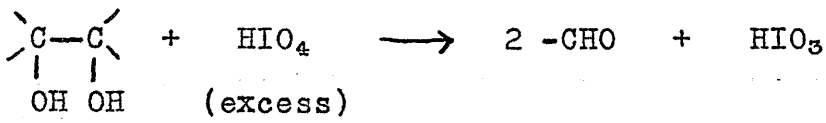
Calculated: 10.52

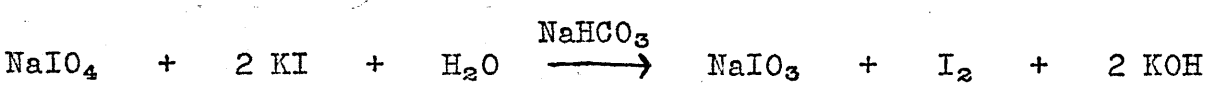
PART VI

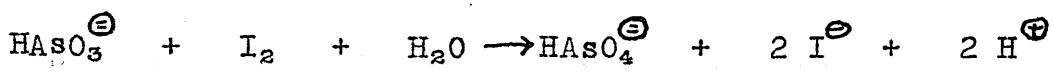
The Determination of Oxirane oxygen

with Periodic Acid









This method of determining oxirane oxygen has been applied to ethylene oxide by Eastham and Latremouille.[32] It has been extended here to 9 other epoxides. All of the reactions involved are well known.[34,35,36] The epoxide was first hydrolyzed to a glycol by water in the presence of acid. This glycol was then cleaved by periodic acid to give two aldehydes and the excess periodate was reduced to iodate in neutral solution by reaction with potassium iodide. It was mandatory that the solution be neutral or slightly basic in this step since, in acid solution, iodate reacts with iodide to give free iodine[63] and in strongly basic solution, iodine reacts with hydroxl ions.[64] Since it is an equilibrium reaction, an excess of arsenite was added along with the potassium iodide to remove the iodine as it was formed and shift the equilibrium to the right. The excess arsenite was then

titrated with standard iodine solution using a starch indicator.

The per cent oxirane oxygen was calculated by the following equation:

$$\% \text{ oxirane O} = \frac{(P - A + I) \times 16}{1000 \times 2 \times W}$$

where P = milliequivalents of periodic acid used.

A = milliequivalents of sodium arsenite used.

I = milliequivalents of iodine used.

W = weight of sample in grams.

For 1,2-3,4-diepoxybutane, a factor of 2/3 was inserted because it requires 3 moles of periodate per mole of epoxide and each mole of epoxide contains two moles of oxirane oxygen.

Preparation of Standard Solutions

Sodium Arsenite Solution

The approximately 0.1N sodium arsenite solution was prepared from primary standard arsenic trioxide (As_2O_3). About 4.700 g. was weighed accurately and dissolved in 40 ml. of 1 N sodium hydroxide. The solution was carefully neutralized with 1 N hydrochloric acid, buffered with 20 g. of sodium bicarbonate and diluted to 1 liter in a volumetric flask. The exact normality was calculated.

Iodine Solution

About 12.7 g. of reagent grade iodine and 40 g. of potassium iodide were dissolved in 25 ml. of water and diluted to 1 liter. The approximately 0.1 N solution was standardized against the standard arsenite solution.

Periodic Acid Solution

A 1.0 N solution of periodic acid was prepared by dissolving 125 g. of paraperiodic acid (H_5IO_6) in 1 liter of water. It was standardized as follows: A 2 ml. sample of the periodic acid solution was pipetted into an erlenmeyer flask containing 10 ml. of water. The solution was neutralized with sodium bicarbonate (1.5 g.) and an excess (usually 25 ml.) of 0.1 N sodium arsenite solution was added followed by 1 ml. of 20% aqueous potassium iodide. After standing at room temperature for 15 min., the excess arsenite was titrated with standard iodine solution using starch as the indicator.

Three days after making up, the s olution began to smell of ozone and after 2 weeks it gave low results.

Analytical Procedure

The sample of epoxide (about 0.008 mole) was weighed accurately into an erlenmeyer flask. To this was added quickly 25 ml. of standard periodic acid solution and 0.4 ml. of 70% perchloric acid[a] by means of pipettes.[b] The flask was stoppered, swirled a few times and allowed to stand for 3 - 5 hr. At the end of this time, the solution was neutralized with sodium bicarbonate (1.5 g.) and the excess periodate was determined by the same procedure used in standardizing the periodic acid solution.

All compounds used were distilled personally before use except 1,2-epoxybutane, cyclohexene oxide and 1,2-3,4-diepoxybutane. The first two were prepared and purified by other students. The latter compound was bought from the Eastman Kodak Company and used as received.

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a. Eastham and Latremouille[52] found that perchloric acid increased the rate of the reaction more than sulfuric.

b. In the case of styrene oxide, 25 ml. of dioxane was also added to bring the reactants into solution.

TABLE I

Data from Oxirane Oxygen Determinations

N of I_2 = 0.0995 N of HIO_4 = 0.871

Run	Compound	W	N of Ars.	ml. of Ars.	ml. I_2
1	2,3-epoxy-	0.4755	0.1278	87.13	26.31
2	butane	0.5020	0.1278	64.91	3.09
3	1,2-epoxy-	0.4753	0.1055	77.41	1.59
4	butane	0.6490	0.1246	49.47	26.22
5[a,c]	1-methoxy-	0.9263	0.0951	62.20	6.03
6[a,b]	2,3-epoxy-	1.0563	0.0948	46.55	6.00
7	butane	0.5550	0.1055	109.57	5.47
8[a,c]	1-ethoxy-	0.8977	0.0951	72.78	3.50
9	2,3-epoxy-	0.5329	0.1055	124.03	6.01
10	butane	0.6489	0.1055	89.76	4.62
11[a,c]	1-bromo-	1.4551	0.0951	99.00	70.97
12[a,b]	2,3-epoxy-	1.6818	0.0948	93.85	74.73
13	butane	0.9250	0.1055	85.80	0.38
14[a,c]	3-bromo-	1.3668	0.0951	129.75	8.03
15	1,2-epoxy-	1.0437	0.1278	69.73	7.25
16	butane	0.9200	0.1278	88.90	4.49
17	cyclohexene	0.7124	0.1246	59.88	6.29
18	oxide	0.8433	0.1278	49.67	17.28

TABLE I continued

19	styrene	0.6595	0.1358	91.31	5.85
20	oxide	0.7583	0.1358	79.84	5.48
21	1,2-3,4-diepoxy-	0.5440	0.1358	79.61	27.74
22	butane	0.4598	0.1358	99.23	2.05
23	3,4-epoxy-1-butene	0.5150	0.1055	49.60	55.65

a. The normality of the iodine solution was 0.0989.
b. The normality of the HIO_4 solution was 0.953.
c. The normality of the HIO_4 solution was 0.791.

TABLE II

Results of Oxirane Oxygen Determinations

Run	Compound	Time (hr.)	% oxirane oxygen Found	Calculated	% purity
1	2,3-epoxy-	4	22.32	22.22	100.4
2	butane	4	22.00		99.2
3	1,2-epoxy-	4	23.10	22.22	104.0
4	butane	3	22.40		100.8
5[a]	1-methoxy-	1	12.50	15.67	79.9
6[a,e]	2,3-epoxy-	3	15.15		96.8
7[b]	butane	4	15.50		99.2
8[c]	1-ethoxy-	1	11.77	13.78	85.4
9[c]	2,3-epoxy-	4	13.93		101.2
10[c]	butane	2.5	13.62		98.8
11	1-bromo-	1	9.56	10.52	91.0
12[e]	2,3-epoxy-	3	10.61		100.9
13	butane	4	11.02		104.7
14	3-bromo-	1	4.82	10.52	45.8
15	1,2-epoxy-	5	10.40		98.9
16	butane	5	10.30		97.8
17	cyclohexene	3.5	16.77	16.67	100.6
18	oxide	3.5	16.28		97.8

TABLE II continued

19[d]	styrene	5	12.10	13.10	93.2
20[d]	oxide	5	12.10		93.2
21	1,2-3,4-diepoxy-	5	34.90	37.20	93.9
22	butane	5	35.20		94.7
23	3,4-epoxy-1-butene	3	32.80	22.90	143.2

a. Prepared from crotyl alcohol via methyl crotyl ether.
b. From the reaction of 1-bromo-2,3-epoxybutane and sodium methoxide.
c. From the reaction of 3-bromo-1,2-epoxybutane and sodium ethoxide.
d. In 25 ml. of dioxane.
e. One ml. of sulfuric acid used in place of perchloric acid.

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